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56 FEBRUARY, 1950 Number 2

CONTENTS

GENERAL MEDICINE

illin Treatment of Early Syphilis—First Patients After Six Years—*J. F. Mahoney, R. C. Arnold and Ad Harris*.... 67

omycin. A New Treatment for Syphilis *R. R. Willcox* 69

omycin and the First Attempts of Its e in Syphilis—*Léon van Lierde* 70

ital Outbreak of Enteritis Due to Duck gs—*Lawrence P. Garrod and M. B. Ilroy* 72

er Nephron Nephrosis. Carbon Tetrachloride Poisoning with a Report of 3 ses—*Charles J. McGee*..... 74

Blood Coagulation in Myocardial Infarction—*Ricardo Raúl Reca*..... 79

ry Tuberculosis Caused by Intravenous f Injection of Tubercle Bacilli, Treated ccessfully with Streptomycin Therapy—*wald R. Jones, Warren D. Platt and is A. Amill* 80

romycetin in the Successful Treatment Recurring Epididymitis—*F. H. Redell* 83

Factors Promoting Erythropoiesis. Significance and Applications—*P. Boni*..... 85

ptoms Attributable to Cold Hemagglutination. Report of 2 Cases—*Jeanne C. nteman* 86

cute Bacterial Endocarditis Due to *Salmonella Typhimurium*—*J. de Swiet* 89

tomycin in the Treatment of Subacute cterial Endocarditis — *Robert Wallach d Norman Pomerantz* 90

ote on the Dosage of Quinine To Be dministered in Acute Malaria—*Ch. W. Winckel* 91

tomycin in the Treatment of Tuberculus Sinuses. Review of 11 Cases — *Harvard Davis* 92

Considerations to the Problem of the Associated Coronary and Cerebral Syndrome —*Cornelio Fazio* 93

The Diagnostic Significance of "Burr" Red Blood Cells—*Steven O. Schwartz and Salvatore A. Motto* 94

The Present State of Physiopathology and Treatment of Seasickness — *Joaquín San Antonio Alvarez* 96

Chloromycetin in the Treatment of Typhoid Fever. Fourteen Cases Treated in the Middle East—*A. T. Cook and D. E. Marmion* 97

Local Action of Oxygen in Burns—*Arturo Montoya Miranda* 99

Variation in the Duration of Tuberculin Skin Sensitivity Produced by Two Strains of BCG—*Ralph F. Jacox and Gordon M. Meade* 101

PEDIATRICS

Acute Respiratory Infections in Infants—*R. E. Bonham-Carter*..... 103

Hemorrhagic Manifestations in the Newborn —*Eleodoro Peña Ramos* 107

Acute Mastoiditis in Children Treated with Penicillin and Sulphadiazine—*A. J. Moffett and G. A. Dalton* 110

Epidemic Diarrhea of the Newborn—*Raul Ortega, Daniel Campos and Jose C. Quiroga* 111

Management of the Premature Baby—*Alan Moncrieff* 113

Clinical Observations in Meningococcic Meningitis—*M. Dominguez Recio*..... 115

SYMPOSIUM SECTION

Etiology of Rheumatic Fever 118

EDITORIALS

Duck Eggs 120

A Third Coronary Artery 121

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General Medicine

icillin Treatment of Early Syphilis –First 4 Patients After Six Years — IAHONEY, J. F., ARNOLD, R. C. AND ARRIS, Ad — *Journal of Venereal isease Information*, 30: 350 (December) 1949.

More than six years have passed since then newly developed antibiotic, peni-n, was first employed in the manage-t of early syphilis. The preliminary rt was presented in October 1943 and based upon the findings in a group of tients. . . . It is desired to place on rd the details of the post-treatment ob-ations of the 4 patients.

The members of the group were young s. Each displayed a reasonably char-ristic lesion of primary syphilis, the tion of the lesion not exceeding 10 ; in any. In each instance, *Treponema idum* was demonstrated by a dark examination of secretion from the le-. Varying degrees of serologic reaction e present at the time of the inaugura-of treatment, but all patients were well the seropositive phase at the com-ion of therapy. There were no histories previous syphilitic infections.

The serologic routine has remained the e for follow-up as it had been for nosis. A battery of accredited Ameri-tests has been employed, and quanti-ns have been carried out with two hods, Kahn and Mazzini. Quantitation he complement fixation test was dis-inued early in the period of post-treat-t observation. All of these procedures e been maintained, as far as possible, at same level of reactivity, and all have n performed in strict accordance with technical dictates of the several orig-ors. In the detection of evidence of tment failure, a reasonably complete lical examination was conducted when-possible, and reliance was placed on serologic tests on the basis of the strong probability that serologic evidence of relapse will precede, or at least accompany, a clinical relapse.

"Treatment consisted of the intramuscular administration of 25,000 units of an amorphous penicillin preparation at four hour intervals for a total of 48 injections. The routine required 1.2 million units of the antibiotic and a treatment period of eight days.

"No additional treatment for syphilis was received by any of the patients except that which will be mentioned in connection with patient 4.

"Follow-up in 3 members of the group was not as regular as might be desired. In a measure this was due to the fact that the patients were seamen and that the period of observation included two of the war years, during which the activities of most young males were not left to their personal discretion. However, all the members of the group were brought under observation recently. As the findings at the beginning of the lapsed periods were the same as those displayed upon resumption of observation, it seems reasonable to assume that the interim findings would have been of the same general character.

"Spinal fluid examinations have been made of material from each patient without any evidence of abnormal changes."

Chart 1 displays data concerned with the diagnosis, treatment, and post-treatment observation of the first patient treated with penicillin. "At the completion of therapy on the eighth day, all serologic tests were positive. By the eightieth day, all serologic tests, with the exception of the Mazzini, had become negative, and no significant degree of positivity has since been recorded. There was a lapse from observation of 28 months; negative serologic findings were recorded prior to the lapse and again upon the resumption of observation. At the time of the last observation, 74 post-treatment months, the

Chart 1

Patient 1	L. W., white, male, 27 years old.
History	Treated for gonorrhea in 1935—no relapse. Negative serology April 15, 1943. Incubation—23 days.
Chancre	Penile, dark field-positive.
Diagnosis	Primary syphilis—9 days.
Treatment	25,000 units penicillin every 4 hours for 48 injections; date begun: June 21, 1943.
Reaction	Transitory macular rash over torso and thighs. Temperature: 38.5° C. 7 days—ulcer healed.

Chart 2

Patient 2	E. D., Chinese, male, 24 years old.
History	No previous venereal disease. Incubation—48 days.
Chancre	Penile, dark field-positive.
Diagnosis	Primary syphilis—10 days.
Treatment	25,000 units of penicillin every 4 hours for 48 injections; date begun: June 28, 1943.
Reaction	Malaise, headache; temperature: 38.2° C. Enlarged, painful inguinal glands. 12 days—ulcer healed.

Chart 3

Patient 3	H. J., white, male, 21 years old.
History	Chancroid 8 months previous; three negative blood tests since. Incubation—31 days.
Chancre	Penile, dark field-positive.
Diagnosis	Primary syphilis—8 days.
Treatment	25,000 units of penicillin every 4 hours for 85 injections; date begun: June 29, 1943.
Reaction	Malaise, headache; temperature 37.5° C. Acute edema of prepuce and pain at base of lesion.

Chart 4

Patient 4	S. I., Negro, male, 18 years old.
History	8 gonorrheal infections between 1936 and 1943. Incubation—39 days.
Chancre	Penile, dark field-positive.
Diagnosis	Primary syphilis—8 days.
Treatment	25,000 units penicillin every 4 hours for 48 injections; date begun: July 6, 1943.
Reaction	Mild systemic Herxheimer 6 hours after start of treatment. 10 days—ulcer healed.
Basis for retreatment	1. Development of gonorrheal urethritis, 273 post-treatment days; treated with penicillin.
	2. Development of dark fi positive lesion on lower 303 post-treatment d ulcer healed on three h dred and ninth day.
Retreatment	40,000 units penicillin ever hours for 60 injections— days after original therapy
Remarks	13 gonorrheal infections tween ninth post-treatment and fifty-second post-treatm month.

patient was clinically and serologic negative."

Chart 2 displays the diagnostic treatment data for the second patient. " of the serologic tests were negative by fiftieth day. At the completion of 785 d of post-treatment observation, the pati was still clinically and serologically ne tive. Then there was a 41 month la from observation. Finally the patient located and again brought under obser tion, 67 months after therapy. The clini and serologic picture was negative bef and after the lapse, and has remained through the seventy-second month of servation."

Information for the third patient shown in chart 3. Following treatme there was a rapid reversal of the serolo tests to the negative phase. The pati was clinically and serologically negat at the completion of 223 days of po treatment observation. A 43 month la from observation occurred, during wh it is believed the serologic reaction mained negative, since it was negative b preceding and following the lapse. The tient was clinically and serologically n ative at the end of 72 months of po treatment observation.

"In chart 4, the record of the fourth tient presents one of the interesting pects of rapid syphilotherapy—reinfecti All serologic tests were recorded as ne tive on the seventy-first post-treatm day, but a return to the positive reacti was noted on the two hundred and eigh sixth day. A dark field-positive lesion developed on the lower lip. The pati was retreated with a more intensive pe cillin schedule. During the course of th apy, the serologic titer reached a h level and then declined. The serologic cu remained in the doubtful zone for so

but did not return to a high titer level. ests were recorded as negative on the hundred and ninety-second day and ined so up to the last observation, nonths after the initial therapy."

The effectiveness of penicillin in the ment of early syphilis has been con- ed by six years of post-treatment ob- ation of the 4 patients who were the ect of the preliminary report on the cillin treatment of early syphilis."

eomycin. A New Treatment for yphilis — WILLCOX, R. R. — *British Iedical Journal*, 2: 1076 (November 2) 1949.

ne following case reports indicate aureomycin has a powerful action up- he organism of syphilis. "The patients Bantu Negroes with early syphilis, outhern Rhodesia, and in all of them *onema pallidum* was demonstrable be- treatment. As the supplies of aureo- in available were scanty and the pros- s of an adequate follow-up problem- l, it was considered expedient to a number with small, probably sub- tive doses and to observe the effect ubsequent dark field examination."

Case 1 (Seronegative Primary Syphi- —A native from Portuguese East ca had a typical indurated penile ary chancre with firm rubbery non- er inguinal glands. The Wassermann Kahn blood reactions were negative, a dark field examination of material n from the sore showed *T. pallidum*. May 18, 1949, he was given three mg. capsules of aureomycin at inter- during 24 hours. Twenty-four hours the starting of treatment the dark still showed *T. pallidum*, although greater difficulty. At 48 and 72 hours, ever, none were recovered: At this e he was given a course of penicillin.

Case 2 (Seropositive Primary Syphilis). male Negro from Portuguese East ca presented an indurated fraenal with a developing left inguinal bubo. ically the case resembled a mixed in- on of syphilis and chancroid, and, ough the dmelcos and Frei skin tests negative, Ducrey's bacillus was seen mears from the sore. The dark field, ever, showed *T. pallidum*, and the Wassermann and Kahn blood reactions were positive. He was given five capsules of aureomycin orally over 29 hours (total 1,250 mg.). Twenty-four hours after the onset of treatment *T. pallidum* was still isolated by dark field, but dark field examinations performed daily for the next 16 days were all negative. By the end of this time the sore had healed and the bubo resolved without additional treatment.

"Case 3 (Seropositive Primary Syphilis).—A male Negro from Portuguese East Africa was admitted with a paraphimosis and an indurated fraenal sore with typical syphilitic inguinal adenitis. *T. pallidum* was seen without difficulty in the dark field, and the Wassermann and Kahn blood reactions were positive. He was given three capsules of aureomycin daily for two days (total 1,500 mg.), and although the sore was still unhealed after 17 days no *T. pallidum* was observed at daily dark field examinations during this time. A week later the sore had healed and the patient was discharged for surveillance.

"Case 4 (Secondary Syphilis).—A Nyasaland Negro attended with multiple perianal and penoscrotal condylomas lata with enlarged nonpainful inguinal glands. The dark field from the condylomas showed an abundance of *T. pallidum*, and the Wassermann and Kahn blood reactions were strongly positive. He was given one capsule of aureomycin orally three times a day for two days (total 1,500 mg.). The response was dramatic, and the lesions had healed completely by the fourth day. Daily dark field examinations had been repeatedly negative.

"Case 5 (Secondary Syphilis). — A female native of Southern Rhodesia was admitted with an indurated primary sore of the left labium majus, which was also oedematous. Secondary vulvar mucous patches and vulvar and perianal condylomas lata were also present, the whole being secondarily infected and evil-smelling. *T. pallidum* was seen without difficulty, and the Wassermann and Kahn blood reactions were markedly positive. She was given one capsule of aureomycin three times a day for two days (total 1,500 mg.), response being immediate. The daily dark field examinations were negative for the

ensuing four days, by which time the lesions had healed. She was kept under observation for a further three days; she was then discharged from hospital with instructions to attend as an outpatient. She returned, however, on the twelfth day with a relapse of the condylomas, and was then treated with penicillin.

"Case 6 (Secondary Syphilis).—A female native of Southern Rhodesia was admitted with perivulvar and perianal condylomas lata, from which *T. pallidum* was obtained without difficulty. The blood Wassermann reaction was positive. She was given four capsules of aureomycin orally (total 1,000 mg.), and the lesions healed rapidly. Daily dark field examinations were negative for the ensuing three days, and on the fourth the lesions had healed.

"Case 7 (Secondary Syphilis).—A male South Rhodesian Negro had a preputial sore from which *T. pallidum* was recovered and secondary condylomas lata on the scrotum. The blood Wassermann reaction was strongly positive. He was given three capsules of aureomycin orally on the first day and two on the second (total 1,250 mg.). Healing was rapid, being complete in four days, during which time daily dark field examinations were negative.

"Case 8 (Seronegative Primary Syphilis).—A male native of Southern Rhodesia had a giant fraenal chancre with typical syphilitic glands. The dark field examination for *T. pallidum* was positive and the blood Wassermann reaction was negative. He was given six capsules of aureomycin orally in 48 hours (total 1,500 mg.). Daily dark field examinations were negative during the next three days and the sore had nearly healed by the fourteenth day.

"Case 9 (Secondary Syphilis).—A male South Rhodesian Negro had an ulcerated prepuce with massive condylomas lata of the scrotum and inner thighs. *T. pallidum* was found on dark field examination, and the blood Wassermann reaction was positive. He was given six capsules of aureomycin orally (1,500 mg.) over 48 hours. Although the dark field showed scanty *T. pallidum* at 24 hours, none was observed at two and three days. At two weeks, information was available to the effect that the condylomas had not disappeared but were quite dry."

Aureomycin and the First Attempts Its Use in Syphilis — VAN LIE LÉON — *Ars medici*, 4: 953 (Noven 15) 1949.

Aureomycin is a yellow powder av able in capsules of 50 and 250 mg. has a bacteriostatic and bactericidal tivity against numerous gram-positive gram-negative germs, like pneumoco *Staphylococcus aureus*, *Streptoco pyogenes*, gonococcus, meningococcus, bacilli of typhoid and paratyphoid fe and *Bacillus coli*, and also against cer viruses like that of Nicolas-Favre's ease, and the Rickettsiae of exanthemat typhus, Queensland fever and Ro Mountain spotted fever. One writer dem strated that aureomycin has a sligh more marked antispirochetic effect t penicillin against *Borrelia novyi* *Leptospira icterohaemorrhagiae*. Acti against *Proteus vulgaris* and *Pseudomo aeruginosa* has not been demonstrated

Aureomycin is soluble but irritating cause of its acid reaction (with a *pH* between 4 and 5); contrary to other a biotics it is not administered intramus larly. Dissolved in a special medium a administered intramuscularly it has p voked anemia and hemoglobinuria; f acid would have a protective value association with the aureomycin dissol in physiologic saline solution. Aureomy is active perorally; the basic dose is to 100 mg. per Kg. body weight per d and the drug should be administered intervals of four to six hours. Intraveno ly aureomycin has given satisfactory sults in doses of 200 to 500 mg. in 2 to 500 cc. of saline solution at interv of 4, 6, or 12 hours; this solution is jected rather rapidly. Local irritation the veins is to be feared but it is l marked than that on continuous infus of penicillin and arsenicals. Whenever patient is incapable of ingesting the d the intravenous injection is the meth of choice.

Inconveniences of aureomycin inclu nausea, vomiting, diarrhea, anorexia a abundant salivation on peroral admin tration, and symptoms of avitaminosis due to destruction of the intestinal flo these symptoms can be controlled diminution of the dose or discontinuati of treatment; there are no toxic symptom

ureomycin passes rapidly into the emic circulation; after peroral admin- ation of 0.75 to 1.0 Gm. every six to t hours the serum will show a level 2 to 4, and sometimes 8 micrograms cc. and this level will persist for some e.

t takes 19 to 30 hours before all traces the drug have disappeared from the od, and this is surprising as nothing he kind has been observed with any the other antibiotics. The "saturation shold" is never exceeded in spite of ease or prolongation of administration there is no cumulative effect. The imal dose has not been established.

ureomycin passes into the tissues and anic fluids, like the cerebrospinal fluid re it reaches a therapeutic level, the ural fluid, the placenta where it is found the fetal circulation, the spleen, kid- s, lungs and liver, the latter excreting vith the bile.

ureomycin appears rapidly in the urine is excreted continuously for two to e days after a single dose of 500 or mg. A concentration of up to 256 rograms per cc. has been found from second to the sixteenth hour; the ary excretion is highest between the rth and eighth hour and therefore the g is administered at intervals of four six hours.

n Nicolas-Favre's disease doses of 10 40 mg. daily for two weeks proved ly satisfactory, including definite im- vement of the rectal stenoses. Good re- s have been obtained in rickettsial dis- es. Typhoid and paratyphoid fever gen- ly respond well, and blood cultures ome negative after two to three days. brucellosis the results were superior to se of any other treatment and the best lts were obtained with a combination ureomycin in a dosage of 3.0 Gm. and ptomycin or dihydrostreptomycin in a e of 2.0 Gm. daily. Six cases of staphy- ccemia were reported with clinically bacteriologically established penicillin stance; 4 were cured by intravenous ctions of 200 to 500 mg. of aureomycin 50 cc. of saline solution over a period 0 to 15 minutes at intervals of 4, 6 or hours; the peroral dosage was 500, or 1,000 mg. every 4 or 6 hours. Better lts would have been obtained if aureo- mycin would have been used from the beginning, instead of penicillin, streptomycin and, in some cases, small doses of sulfonamides. Cure was reported in a child with desperate mandibular osteomyelitis which was resistant to penicillin and sulfonamides. In conjunctivitis caused by bacteria or viruses a 0.5 per cent solution of aureomycin borate in saline is used. In primary atypical pneumonia which has frequently proved resistant to high doses of penicillin encouraging results have been obtained with doses of 1.5 Gm. every six hours until several days after defervescence. In all cases of pneumococcic pneumonia the temperature became normal 18 to 36 hours after the first dose of aureomycin, and no pneumococci could be demonstrated after two days in the sputum; the results are comparable to those of adequate doses of penicillin or sulfadiazine. Little is known concerning the effect of aureomycin in meningococcic meningitis. In gonorrhea aureomycin is active but not more so than penicillin.

O'Leary and Kierland were the first to use aureomycin in the treatment of syphilis and established the antisyphilitic efficacy of this antibiotic. The first cases were primary syphilis and an average of 400 mg. was given every four hours by mouth; on the fourth day the dosage was increased to 500 mg., and on the sixth and seventh days to 750 mg., and then a dosage of 500 mg. was continued. The total dose was slightly above 40 Gm. In 1 case a Herxheimer's reaction was observed 24 hours after institution of treatment.

Ultramicroscopic examination was negative after 60 hours, and after 96 hours roseola and mucous plaques disappeared and the chancre was on the way to cicatrization. Treatment was terminated between the fifteenth and twentieth day, when all lesions were cicatrized, although induration persisted at the borders of the chancre. The serologic reactions have not yet shown any marked modifications but this is not surprising in the light of the experience with penicillin. Aureomycin also proved effective in several cases of ulceronodular tertiary syphilis, given in doses of 250 mg. for three days, then 750 mg. for two days, and subsequently 1,000 mg., always at intervals of six hours, and up to a total of 50 to 60 Gm. over a period of three

weeks. Lesions dating back 10 years showed transformation from the second to fourth day on and were healed at the end of the period of treatment. The serologic reaction remained positive but the quantitative Kahn titer showed a marked decrease. Peroral aureomycin treatment also proved effective in neurosyphilis; in 5 out of 7 cases the drug could be demonstrated in the spinal fluid, contrary to penicillin. The role of aureomycin in future syphilis treatment cannot be evaluated as yet but its antisyphilitic effect has been established. At present the drug may be used in penicillin resistant or sensitive cases.

True resurrection in a desperate case of true pemphigus was reported within four days after institution of treatment with 500 mg. of aureomycin at intervals of four hours.

Hospital Outbreak of Enteritis Due to Duck Eggs — GARROD, LAWRENCE P. AND MCILROY, M. B. — *British Medical Journal*, 2: 1259 (December 3) 1949.

"On the morning of July 7, 1949, about 40 nurses at St. Bartholomew's Hospital had reported sick with an acute febrile enteritis, and many patients throughout the wards of the hospital were similarly affected. Inquiry in the kitchen revealed that a lightly cooked pudding containing 200 duck eggs had been served to the nursing and other female staff and to patients on July 5. It was therefore no surprise when stool cultures revealed the presence of *Salmonella typhimurium*."

"The incriminated dish was a 'queen of puddings.' In preparing this, yolks of eggs are beaten up with milk and added to bread crumbs in dishes in which the mixture is baked for 35 minutes, during which it becomes semisolid. It is then smeared with hot jam and covered with a layer of beaten-up white of egg mixed with a boiling saturated solution of sugar. The pudding is then returned to the oven for five minutes to brown this top layer. The whole of a consignment of 200 duck eggs had been used to make this pudding: none of these were left, nor was any of the pudding itself, when its effects became manifest two days later. That it was the cause was proved conclusively by its effects on the family of a member of the kitchen staff who took some of the pudding h and gave it to them: these persons admitted to another hospital, and *S. ty murium* was recovered from their sto

"It was found that the duck eggs been collected by the wholesaler from farms in Essex, at 2 of which conditi were reported by the local health aut ities to be insanitary.

"This pudding was served in the nu dining room, where certain other fe staff also take their midday meal, an patients throughout all the wards. amount prepared was said to suffice 700 portions, but it is impossible to s how many people ate it, because an al native sweet was also served.

"Varying numbers of patients in alm every ward of the hospital were affec totalling about 60. A few, owing in p to their previous condition, were grav ill, and 1 elderly woman died. That c paratively few patients were attacked due to the preference of the average h pital patient for rice pudding, the al native sweet served." It was impractica to follow all these cases, and this acco will deal in detail only with the dise as seen in the nursing and domestic sta

"Attack Rate.—At the time of the o break the nursing and domestic staff nu bered 351; of these, 197 ate the pudd and 136 were affected; 154 did not the pudding and 11 were affected. Of th who ate the pudding 59 out of 136 w sufficiently ill to report sick.

"Incubation Period.—The time of on of the first symptom was determined the nearest hour by direct inquiry or a questionary distributed within a we of the start of the epidemic. Opinio differ on the limits of the incubation peri of *S. typhimurium* enteritis. . . . In t present epidemic there were a number secondary cases, and it is difficult to defi the upper limits of the incubation perio but of 136 persons who ate the puddi and were ill, 120 noticed symptoms with 48 hours. The mean incubation period w 23.8 hours in these cases. Of the remai ing 16, 3 had an incubation period of 9 96 hours: they are considered secondar infections. There is not enough eviden to be sure whether the remaining 13, wit incubation periods of 48-76 hours, we primary or secondary infections.

Secondary Infections.—The 11 who developed symptoms without having eaten pudding require further explanation. The pudding was the source of infection, either their evidence was incorrect or were infected secondarily. All 11 had clinical symptoms and 4 had positive stools. These had incubation periods of 42 hours more and could be secondary cases. The remaining 2, who were ill 23 and 27 hours after the pudding was served, ate lunch in the main dining room on the day in question, but said they did not eat the pudding. One had a positive stool culture: the stools of the other were not examined until after recovery, when they were negative. It is just possible that these 2 were served the alternative sweet with a spoon used for the infected pudding. The total number of secondary infections among nurses and domestic staff is thus thought to be 12, including 5 with positive stools. There was ample opportunity for cross infection, since many nurses were looking after affected patients in the wards. Secondary infections also occurred among the patients. Four patients in different wards developed *S. typhimurium* enteritis 4, 6, 7, and 21 days after the start of the epidemic. All 4 had positive stools. The latest secondary case was that of a woman who was ill two months after the epidemic. She was thought to have contracted the infection from a baby born during the epidemic which was infected by its mother and continued to excrete bacilli for several weeks. Another secondary attack was produced in an unusual way: it occurred when a physicist who was performing estimations of the radio-iodine content of the faeces of a patient with thyrotoxicosis unfortunately contracted the infection.

Symptoms.—The presenting symptoms of the 136 persons who ate the pudding and were ill were as follows:

Abdominal pain	37	patients
Headache	27	"
Diarrhoea	22	"
Nausea and vomiting	12	"
Shivering	11	"
Malaise	10	"
Backache	9	"
Giddiness	3	"
Dizziness	2	"
Faintness	1	patient
Stiff neck	1	"
Fever	1	"

It will be seen that abdominal pain, headache, and diarrhoea were the commonest. The disease was more closely studied in the 59 who reported sick; in 48 of these stool cultures were positive. Fever occurred at some stage of the disease in 55, and 48 had a temperature of over 100° F. The average duration of fever was 3.1 days, and the longest 7 days. Diarrhoea with three or more stools a day was present in 45, and the largest number of stools per day was 26. The stools were watery, with mucus but no blood. No green stools were reported. Vomiting occurred at some time in 18, usually at the onset. Abdominal pain was almost invariably present, and was colicky. Three nurses developed transitory urticarial rashes while they were ill, and 1 ward maid had an epistaxis. The average duration of illness in the 59 cases reporting sick was 6.1 days; the longest was 12 days. In 10 cases there were sequelae—in 3, mild diarrhoea persisted for two to three weeks; 5 had a further mild gastrointestinal upset lasting two to three days in the next four weeks; and 2 of the more severely ill complained of weakness and lassitude during the next month. Stools examined during these possible relapses were all negative.

"Treatment.—All cases reporting sick were given sulphaguanidine or sulphasuxidine, 3 Gm. at once and 1.5 Gm. six hourly, without obvious effect. Three of the more severely ill nurses were given streptomycin by mouth in 0.5 Gm. doses four hourly: this treatment was also given to several very ill patients, and was considered to have had a good effect. The organism was shown to be streptomycin sensitive, being inhibited in vitro by a concentration of 1 μg. per ml.: in an infant similarly treated the organisms still present in the stools after recovery were found to be highly resistant. If streptomycin is used in this disease it should evidently be given by mouth. It is of interest in this connexion that 2 patients under treatment with intramuscular streptomycin for tuberculosis developed enteritis in spite of it, although in 1 of them the attack was mild and somewhat atypical."

"Examination of Faeces.—Cultures of specimens from some of the original cases and certain others in the acute stage were made on desoxycholate-citrate medium and

MacConkey's medium. No attempt was made, or could in the circumstances be made, to confirm the diagnosis in all the cases at the height of the epidemic, which accounts for the fact that positive stool cultures were not obtained in all evident cases discussed in the foregoing analysis. On the other hand, it was imperative to examine faeces from all affected nurses after recovery to be sure that none remained a carrier. Many had to return to duty before this had been done, and some had gone on more or less prolonged sick leave or annual leave; but arrangements were made to obtain a series of specimens at intervals of not less than four days from all affected nurses, until at least two negatives had been obtained. (Kitchen and other domestic staff and, so far as possible, affected patients were examined similarly. These examinations continued for several weeks and raised the total of specimens dealt with in connexion with the outbreak well into four figures.) Such specimens from convalescents were cultivated solely by the heavy inoculation of a tube of tetrathionate medium, which was plated after overnight incubation.

"These specimens were obtained at such irregular intervals that no adequate data exist for a detailed analysis of the rate of disappearance of the organism. The findings, such as they are, may be summarized by saying that almost all specimens examined during the first week were positive: the number of known positives fell by the end of the second week to 12 and after a third week to 4; thereafter only 1 positive culture was obtained (on the twenty-second day). (These figures refer to nursing and domestic staff only: several patients, including 2 infants, carried the organism for longer periods.)

"Agglutinin Formation.—The blood of 12 nurses was examined for agglutinin during convalescence, in most cases about two weeks after the onset. Agglutinin for *S. typhimurium* was found in all but 1, the titre varying from 1 in 25 to 1 in 500: there was a strong suggestion that a higher titre was reached after a more severe attack.

"Cooking Experiment.—With the kind cooperation of the catering officer, a pudding identical to that responsible for the outbreak was inoculated with culture of *S. typhimurium* and cooked in the way, cultures being made from it wards. The object was to produce in egg-containing parts of the pudding a terial content of about 100,000 orga per ml., and viable counts before co showed that this had been achieved i lower layer (yolk of egg and milk was not thought advisable to add cu to the white of eggs before beating the addition of boiling sugar solu owing to the danger of contaminating power-driven machine used in the prep tion of this material, and after its prep tion it was difficult to achieve uni admixture of a small amount of a liquid. Moreover, this is a material which it is almost impossible to quantitatively. This part of the experi was therefore not wholly satisfactory

"The results can be expressed sh by saying that whereas before cooking constituents contained the organism the former case in very large and ascert ed numbers, afterwards both were al completely sterile, and from neither stituent in any of many cultures wa *typhimurium* recovered."

Lower Nephron Nephrosis. Car Tetrachloride Poisoning with a port of 3 Cases — McGee, Char J. — *American Journal of the Med Sciences*, 218: 636 (December) 19

"Lower nephron nephrosis is seen association with renal damage follow intravascular hemolysis due to sulfo mides, quinine and other antimalari arsine, abortifacient pastes, due to action of the soaps on the blood and int venous water, incompatible transfusi diabetic coma, concealed hemorrhage, p longed labor, operations on the biliary tra pneumonia, scarlet fever and diphthe blackwater fever, transurethral prostat tomy, crush syndrome, nontraumatic m cular ischemia, electrical injury to mus heatstroke, ureteroplacental damage, alkalosis from excessive emesis, therm burns and volatile poisons, especially c bon tetrachloride, bleeding into the gast intestinal tract, Porro cesarean, possi also with toluene and rarely following m curial diuretics."

gestion of carbon tetrachloride s first the liver with apparent spar- f the kidney. Inhalation damages rily the peripheral vascular system ich the kidney is a component."

ith or without shock, depending on iological factor, the patient develops a, vomiting, weakness, malaise, some- pain in the abdomen or back, and rapidly or insidiously, oliguria or a. Following this there is the develop- of edema (the degree of which will d on the treatment), a rising blood re, rising nonprotein nitrogen and sis, and death may intervene from pulmonary edema or potassium in- tion. During the course of the illness may be marked nervousness and lousness. During acidosis, tetany d not develop, although total calcium diminish. Calcium therapy must be lly watched in this disorder."

addition to chemical changes one must remember that there is a definite rrhagic tendency as seen frequently body fecal discharges, ecchymoses and ura.

n the treatment of these patients it be remembered that they will lose only by evaporation and in the ex- air, a total of about 1,000 cc. daily. use of gastric irritation, oral feeding is uded and very shortly the slight car- drate reserves are exhausted. Then tion depends on protein and fat metab- approximately 70 and 200 Gm. re- ively daily, with resultant ketosis, mia and increasing potassium, sul- and phosphate wastes. From the bolism of these body stores there will pproximately 500 cc. of preformed r and water of oxidation. The average has roughly a 50 liter 'pool' of fluid s body in which to dilute these rising e products. . . . It is dangerous to these patients with intravenous saline use this further increases the electro- concentration within the 'closed' m and further increases the acidosis. ose aids metabolism of fats by curtail- etosis."

cessive fluid must be avoided in a way system, or pulmonary edema and n will result.

eritoneal lavage has had its advocates. he early stages of peritoneal lavage there is excellent removal of nitrogenous waste products. The experience of those who have used it indicates a decreasing dialysis of nitrogenous waste products proportional to the duration of the total lavage, peritonitis and mechanical difficulties with the apparatus. One must also consider the huge quantities of fluid passing through this system which may produce disastrous changes in the electrolytic and water balance. The initial enthusiasm for this procedure has markedly abated in recent years."

"The use of calcium therapy is stressed in this syndrome."

Case Reports.—Case 1: E.B.I., a male, age 22 years, was admitted to hospital April 1, 1948, for generalized aches and pain, nausea and vomiting.

"The past history revealed the usual childhood diseases and influenza with hospitalization in 1947. The family stated that the boy began drinking heavily after discharge from the Navy in 1946 and that he was in the habit of going on periodic drinking sprees for several weeks at a time.

"The present illness dates back to March 30, 1948, when 3 men cleaning offices used carbon tetrachloride to mop the floor. After 15 minutes of this the patient complained of headache and for the next 45 minutes walked in and out of the room. At the end of this time the 2 other men complained of headache and slight dizziness which disappeared soon after discontinuing the use of the chemical. When the patient started working at 4:00 P.M. on March 30, 1948, he complained to his companions that he had been sick on the preceding day and that he did not feel well on reporting to work that evening. On admission he was under the influence of alcohol and it was learned that he had had an extended alcoholic 'binge' on the preceding evening.

"Physical examination showed a moderately well developed white male complaining of vague muscular aches and pains but not critically ill. The nose and pharynx were slightly injected and there were tender and slightly enlarged submaxillary nodes in the neck. The eyes, ears, lungs, heart, extremities and reflexes were not remarkable. There was rigidity in the right side of the abdomen and an enlarged liver. Extremities and reflexes were normal, skin

was dry. Temperature was 99.4° F., pulse 86, respirations 20, blood pressure 120/70.

"The laboratory findings on admission showed hemoglobin of 14.5 Gm., 4,700,000 red blood cells, 16,150 white blood cells (95 per cent neutrophils and 5 per cent lymphocytes); by the 5th of April, 12.5 Gm. of hemoglobin, 3,890,000 red blood cells with slight anisocytosis. No urine was obtained until the 4th of April when it showed a specific gravity of 1.019, acid reaction, 2 plus albumin, 1 plus sugar, 1 to 2 white cells, few epithelial cells and much amorphous material in the sediment. On the following day the urine showed a specific gravity of 1.012, alkaline reaction, 4 plus albumin, no sugar, 20 to 25 white cells, 0 to 2 red cells per high power field, 1 finely granular and 0 to 2 coarsely granular casts.

"On the second hospital day the blood pressure rose to 152/110. He was given rather copious amounts of intravenous fluid because of vomiting and anuria. On April 2 he received 2,000 cc. of intravenous fluids, 2,500 cc. on the 3rd and 4,500 cc. on the 4th.

"A surgical consultation was held on April 4 because of the persistent emesis, marked distention and rigidity of the entire right abdomen. At the suggestion of the surgeon, Wangensteen suction was instituted without any relief. The patient continued to vomit around the tube, even though the suction was draining well.

"Early on the morning of April 5, he began to spit and vomit bloody mucus, became quite drowsy and edematous. During the day he continued spitting considerable bloody froth. Oxygen was administered by tent. At 6:00 P.M. the blood pressure was 170/0, the edema was increasing hourly. At 8:00 P.M. the blood pressure was 190/40. A venesection for relief of the pulmonary edema was unavailing. Petechiae were noted at this time in the conjunctivas. Slight temporary improvement in the respirations was obtained late that night by the use of 50 cc. of 50 per cent glucose with 0.5 Gm. aminophylline intravenously. This procedure was repeated at 1:00 A.M. on April 6. At 6:30 A.M. the blood pressure had risen to 170/80, and the pulse was full and strong. The edema of the face had completely disappeared but there were coarse bubbling rales throughout both bas 11:45 A.M. he had a slight conv vomited a copious blood-stained flu came cyanotic and died at noon. the entire hospital stay he had r 30,000 units of penicillin intramus every three hours.

"The urinary output was not me until the 4th at which time he ha cc. of urine and 1,150 cc. of emes the 5th he had a urinary output cc. and 1,900 cc. of vomited fluid."

Specimens of the liver, kidney lung tissues were sent to labor Volatile organic chlorides were fou each specimen submitted; but no d quantitative data were available. mens were also sent to a second who found severe central necrosis lobules of the liver and interstitial and hydropic degeneration of the t of the kidney, which findings he th were consistent with carbon tetrach poisoning. Specimens sent to a third tor were reported upon as follows: " sections from the liver and kidne entirely characteristic of carbon chloride poisoning. The liver sho sharp central necrosis without as ye dence of regeneration. The kidney typical lower nephron nephrosis, pigment casts, degeneration of the as ing limbs of Henle's loop, interstiti flammation at the corticomedullary tion and foci of venous thrombosis. synergistic effect of alcoholism in rel to carbon tetrachloride injury is well e lished, both experimentally and from cal experience. It is very probable th played a contributing role in this case

"Case 2: C. R., a 36 year old, well d oped, well nourished, white male was mitted to . . . . hospital on Decembe 1948, in acute distress, complainin aching in the upper abdomen, and na and vomiting of about 12 hours' dura He had been a rather hard drinker the age of 21 at which time he bega drink 2 to 3 quarts of whiskey we On December 23, 1948, there was a in the insulation around the machine his ice box, for which he used a py fire extinguisher containing 25 per carbon tetrachloride. This procedure pied about five minutes, but because space in which he was working was

2.5 by 2.5 by 0.5 feet, and he was close enough to observe the fire, he ed a very high concentration of carrachloride in these few minutes. He no ill effects that night but on the g of December 24 he began to feel ssed, although he could not describe efinite symptoms. During the morn- Christmas day he had severe pain e epigastrium and back which was ated with frequent and persistent ing, malaise and weakness. Around on Christmas day he began to note ness of both arms. He also complain- distention. He was admitted to the tal by ambulance.

is past history also reveals that he been a dyer for many years. During war he worked as an electrician and ll so employed, and though during war he was in close association with rs he feels that he never was exposed very high nor prolonged concentration xic or metallic fumes. In spite of the us amounts of emesis, he had not l its character, although during the part of the morning he was quite ite that it was only clear fluid. He noticed for some time that on an inient fluid intake, he may note some t urinary burning, but otherwise has ed no abnormalities in the genitourisystem and as regards his slight urioutput during the past few hours, he hat it was due to the copious and perit vomiting. Four years ago when he ed an insurance policy to lapse he was d to have a slightly elevated diastolic d pressure.

The history of carbon tetrachloride oning, though persistently sought, was elicited until about five days after ission when he thought of the fire and fumes.

His height was 68 1/2 inches, weight pounds, temperature 99.4° F., pulse respirations 20 and blood pressure /80. The local physical examination aled a very tender epigastrium with ite rigidity and no rebound. Neither overtebral angle was tender, although irly hard punch on the left side did e some jarring disturbance. The reder of the physical examination was remarkable.

"On admission the urine had a specific gravity of 1.007, acid reaction, 3 plus albumin, no sugar, 0 to 1 white blood cells, 0 to 1 red blood cells, many granular casts and much amorphous material. Hemoglobin was 14 Gm., with 4,500,000 red blood cells, 11,400 white blood cells (99 per cent neutrophils, 1 per cent lymphocyte). Roentgen rays of the chest and flat film of the abdomen in an upright position were not remarkable. The probable diagnosis of penetrating ulcer was entertained and he was admitted to the surgical service.

"Late that afternoon the urine was acid, 3 plus albumin, no sugar, 1 to 3 white blood cells, many epithelial cells, many granular casts and much amorphous material. There were 12,350 white blood cells (98 per cent neutrophils and 2 per cent lymphocytes). No record was kept of the urinary output during the remainder of Christmas day, but on the following day there was no urinary output. There was slight icterus of the scleras. A specimen of urine examined on the 26th, but passed on the 25th, showed an acid reaction, 3 plus albumin, no sugar, 2 to 3 white blood cells, 20 to 30 shadow red blood cells, many epithelial cells and 0 to 3 coarse granular casts. On the 26th the white blood count had risen to 15,600 (96 per cent neutrophils and 4 per cent lymphocytes).

"During the remaining portion of Christmas day he received 2,000 cc. of 5 per cent glucose in saline intravenously. On the 26th he was allowed to have fluids freely by mouth. On the morning of the 27th the urine showed a specific gravity of 1.016, acid reaction, 3 plus albumin, 0 to 2 white blood cells, 1 to 3 red blood cells, a rare finely hyaline cast and 5 to 6 coarsely granular casts. The white blood count was 10,725 (89 per cent neutrophils, 7 per cent lymphocytes and 4 per cent monocytes). The icteric index on the morning of the 27th was 27.5 units, the carbon dioxide combining power 36 vol. per cent, the blood chlorides 400 mg. per 100 cc. and blood urea nitrogen 86.7 mg.

"Inadvertently it was not realized that the urinary output had been zero and an intravenous pyelogram was done on the 27th which failed to show any excretion of the dye in 45 minutes. It was then

realized that something had happened to the kidneys and intensive unsuccessful search was made in the history by numerous observers for definite history of chemical solvent or other toxic substance. Diagnosis of lower nephron nephrosis was entertained and he was transferred to the medical service.

"On the 27th the vital capacity was 3.2 liters, or 74 per cent of normal. There was evidence of fluid in the bases posteriorly. He was placed on a very conservative regimen, receiving 750 cc. of 15 per cent glucose intravenously every 24 hours with sufficient heparin thereafter to prevent clotting of the needles. Vomitus was replaced quantitatively with saline intravenously and fluids by mouth were limited to ice chips at very infrequent intervals, only sufficient to keep the mouth from being uncomfortably dry. On the 28th the blood urea nitrogen was 85.5 mg., blood chlorides 430 mg., thymol turbidity 7 units, albumin globulin ratio 3.98:1.46. Red cell fragility test was normal. There was no clinical evidence of icterus. The blood pressure was 190/80.

"The fluid in the lungs did not change for several days. The blood chloride remained relatively constant at 440 mg., the urinary chlorides were being excreted at the rate of 3 to 4 Gm. per liter.

"On the morning of the 30th the blood urea nitrogen was 91.5 mg., carbon dioxide combining power 50 vol. per cent. During that afternoon the patient had a very severe tonic convulsive seizure during which he bit his lower lip severely and his convulsion did not respond to the usual intravenous sedatives. Intravenous calcium was given, immediately after which he went into a deep and untroubled sleep for about 30 minutes, following which he had no remembrance of the convulsion. The blood calcium at this time was 7.8 mg. and subsequently intravenous calcium therapy was started. The following day, because of some twitching of the face and a positive Chvostek sign, the intravenous calcium was increased to twice daily.

"On the 31st the urine showed a specific gravity of 1.007, alkaline reaction, 4 plus albumin, 0 to 2 white blood cells, a few round epithelial cells. The hemoglobin had dropped to 12.5 Gm., red blood cells to 3,870,000. There were 14,650 white blood cells (82 per cent neutrophils, 8 pe lymphocytes, 8 per cent monocytes, cent eosinophils, 1 per cent baso Blood chlorides were 450 mg. per 1 Two doses of 100,000 units of pe were given intravenously, 12 hours for the infected necrotic patch on th er lip."

"On January 1, the blood urea ni was 98.8 mg. The patient was quite ous and irritable. During this tim up through the 3rd of January the p had been complaining of troublesom tention, but it was felt unwise to giv relief of the distention other than b soapsuds enemas as needed. On th he was passing mucus and blood fro rectum, and hemorrhoids which had relatively asymptomatic, became pa It was apparent that he was bec more edematous and on January 5 blood urea nitrogen was 152 mg. A time the urine was beginning to form and from this time his course may be to follow his changing fluid and electr balance.

"On the 6th the chlorides had dro to 340 mg. and it was decided to give intravenous saline as well as oral so chloride in capsules. Oral sodium chl made him quite distended and uncomf ble. At this time very slight infiltratio glucose had ruined the veins of the a to the point of preventing further in venous medication therein. At no had the veins in the legs been satisfac and a cutdown was not desirable. Ex for troublesome distention in the d shortly after restarting oral food, al the 5th of January, and very painful a the recovery period was uneventful he was discharged on January 17, 194

"He was seen again on January 23, 1 at which time he felt much improved unfortunately had an upper respiratory fection. The blood pressure was 160/1 pulse 100, respirations 14. It was deci at the time to stop his excessive salt int because his urinary output was appro ing 1,500 cc. per day. He was allowed return to light duties. He was seen ag on February 2, 1949, and the blood p sure was 146/94. His improvement been steady and for 10 days he had b at a type of work in which he rated h self at 30 per cent of his former efficie

vas having no urinary difficulties whatr and his total output was about 1,200 er day. On February 25, 1949, he was plaining of headache and stiffness of oints when starting motion, but 'limg up' shortly after motion was be. Otherwise he had regained his former ency at full duties.

Case 3: M. P., a 34 year old white rican housewife, was admitted to . . . . ital on February 3, 1949, with a comnt of nausea, vomiting, diarrhea, genized aches and pains and generalized kness of two days' duration following ld.

The past history revealed the usual dhood diseases, scarlet fever, rheumatic r, 'St. Vitus' dance' and pneumonia in hild form as a child. There have been r or five episodes of acute rheumatic r since. She had a complete hysterecy in June of 1948. There is an exsive alcoholic history.

On admission the physical examination ealed an acutely ill, depressed woman a fair state of nutrition. Her tempera- e was 98.6° F., pulse 84, respirations and blood pressure 110/50. The pupils e miotic, probably as a result of mor- ne. Otherwise the eyes, ears, nose, oat and chest were not remarkable. e abdomen revealed appendiceal and lline incisional scars. The muscles of abdomen were tender throughout. The r was irregular and was felt 3 to 4 cm. ow the costal margin. The region of gallbladder and, or, the liver was quite der. Pelvic examination was deferred. e lymph nodes and breasts were nega- e. The muscles of the extremities ached pressure.

'On admission the blood count was 11.5 n. of hemoglobin, 4,250,000 red blood ls and 20,100 white blood cells (89 per nt neutrophils and 11 per cent lympho- es). There was slight anisocytosis of red blood cells. The Kahn test was gative.

'The temperature at 8:00 P.M. on Febry 3, 1949, was 102° F., pulse 100, pirations 24 and the blood pressure had len to 88/42. At 1:40 A.M. on February it was noted that the patient was bening rapidly worse; she was heard to p for a short while and expired 14 rs after admission to the hospital.

"The internist's original impression was viral enteritis; he wrote 'at the time of examination this morning her clinical condition in no way seemed critical.' The sudden demise of this patient was extremely puzzling in the absence of the history of carbon tetrachloride poisoning and the internist entertained such diagnoses as uremia, pulmonary embolus, cerebral edema, purpuric manifestation in the brain secondary to some virus infection, meningitis, Waterhouse-Friderichsen syndrome.

"After her death the husband related that about four days prior to admission the patient had used carbon tetrachloride to clean the furniture in her trailer.

"At autopsy the body appeared jaundiced. The internal organs and serous fluids were jaundiced. The liver was smooth and very fatty, with marked fatty infiltration of the cut surface. Grossly, the kidneys were normal. The impression was hepatorenal syndrome in the absence of any abnormality of the adrenal glands."

The Blood Coagulation in Myocardial Infarction — RECA, RICARDO RAÚL— *La prensa médica argentina*, 36: 2078 (October 14) 1949.

Embolic complications observed in patients with myocardial infarction led to the assumption of thrombus formation with subsequent detachment as cause of the embolism; at first it was assumed that the emboli originated from the cardiac cavities in connection with the myocardial lesion but later, with increased knowledge of phlebothrombosis, their origin was looked for in the limbs. The situation after an infarction presents favorable conditions for blood intravascular coagulation on the basis of bed rest and fall of blood pressure, and also of factors which cause accelerated blood coagulation, including an alteration of the albumin-globulin ratio from increase of the labile proteins globulin and fibrinogen as evidenced by increase of the sedimentation rate and causing increased capacity of the platelets for agglutination, and an increase of the circulating thrombokinase originating from the necrotic myocardial area. An attempt was made to confirm the increased coagulability in patients with myocardial infarction by means

of the test of Waugh and Ruddick. The first authors adhered strictly to the technic but used only the ninth tube, with 0.7 unit of heparin, and found in a study of 27 cases that increased coagulability almost started after the third day of the thrombotic attack and lasted several days or weeks; in 1 case it did not appear until the twelfth day and the return to normal was also delayed. With the complete technic using all nine tubes the typical curve as described by Waugh and Ruddick was confirmed. Normal conditions were encountered in 16 control cases of other cardiac conditions.

One concluded that the acceleration of blood coagulation exists between the third day and the end of the third week after the infarction, with its peak between the fourteenth and seventeenth day, that the Waugh and Ruddick test is an indirect yardstick of the thrombokinase concentration, that the increase of the thrombokinase is probably not different from that occurring after hemorrhage, muscle injury, trauma and surgical and obstetric interventions, that the acceleration of the coagulation does not play any part in the etiology of coronary thrombosis, but is a result of it and may lead to further complications, and that the ideal method would be one of direct determination of the thrombokinase concentration.

However, other authors did not confirm these findings and an increased coagulability in only 3 out of 15 cases was reported, while the prothrombin time remained normal in 13 and decreased in only 2.

The author studied 2 of his 5 cases at the patients' homes and for this reason anticoagulant treatment could not be instituted once accelerated coagulation was established as daily prothrombin time determinations were not feasible. Tube nine with 0.7 unit of anticoagulant was used in all cases (solution A) and solution B in some cases; the test was always done with three tubes simultaneously. All tubes were kept at a constant temperature of 19° C., but in tests done in the patient's home the temperature ranged between 16° C. and 17° C.

Of the 3 cases in which the diagnosis of infarction was certain 2 showed a definite acceleration of the thrombokinase time, while the third showed only a minimal shortening when compared with the l analysis after three weeks; the time appearance coincided with that given another, and 1 patient died at the ti when the thrombokinase time was short In 2 cases the diagnosis was disputab in 1 of them accleration was definite a in the other which was only studied in later course it was prolonged until af 60 days, coinciding with a prolonged a complicated clinical course. The tests w the B solution showed variable results a confirmed the findings in normal indivi uals; namely, that a test with such cc centrated heparin solutions is of no valu

Repetition of the Waugh and Ruddi test throughout the course of the affecti is of much greater value than a sing determination as the values may vary wit in a considerable range from individual individual, and comparison with the in vidual patient's normal value, as obtain during the first two days after infarctio is necessary. The possible diagnostic val of the test needs further clarification. O case indicated that the hypercoagulabili is related to the size of the infarction an to the prognosis. The significance of t test for the indication of anticoagula treatment and its control requires and d serves further studies. The method is va uable as it is the only one to determi hypercoagulability.

Miliary Tuberculosis Caused by Intravenous Self Injection of Tubercle Bacilli, Treated Successfully with Streptomycin Therapy — Jones, Oswald R., Platt, Warren D. and Amill, Luis A. — *American Review of Tuberculosis*, 60:514 (October) 1949.

"The following is a case study of 30 year old unmarried female, an experienced bacteriologist, who injected herself intravenously with 1.0 cc. of suspension of virulent strain of tubercle bacilli with possible suicidal intent. The injection was made into the left antecubital vein. She stated that she prepared the inoculum by washing a few cubic centimeters of saline over a slant of Petragnani's medium which contained a 14 day growth of *M. tuberculosis*. The culture represented a primary isolation from the pleural fluid of a young man with an acute tuberculous pleurisy

interesting background to this episode the fact that three years previously, le inoculating a guinea pig, she had dentally punctured the skin of her left ecubital fossa with a needle contamied with tubercle bacilli. Following this, noticed a very small superficial papule the puncture site which disappeared r a few weeks and was not associated h further swelling, induration, tender-s, or any systemic symptoms. Previous this episode in 1945, she does not remember having had a tuberculin skin test. e year after the 1945 incident, however, uberculin skin test was positive."

The patient (L. F.) was admitted to pital on January 15, 1948, the day following the intravenous injection, but did reveal any information concerning her inoculation. "Instead, she complained a 5 pound weight loss, night sweats, igue, urinary frequency, 'pus in her ne,' and a chronic nonproductive cough three months' duration. She emphasized fact that she had worked in a Veterans' spital for tuberculosis in 1945.

"The patient was referred to the urology vice with a tentative diagnosis of pyelephritis, possibly tuberculous in origin. r temperature at the time of admission s 101.8° F., which subsided to normal her second hospital day. The patient er stated that her temperature had gone 104° F. a few hours after the injection d was on the way down (101.8° F.) en she was admitted to the hospital. e remained in the hospital for eight days ring which she continued to be afebrile d asymptomatic except for the first day. r blood count, routine urine examinaons, urea nitrogen, and erythrocyte sedientation rate were all within normal nits. A chest roentgenogram showed no normal densities in her lungs. Cystospy revealed the findings of a subsiding fection in the bladder. Pyelography owed pyelectasis and some clubbing of e calyses of the left kidney. Cultures Petragnani's medium) of the urine of the adder and both ureters, however, realed no tubercle bacilli. A guinea pig oculated with a 24 hour urine specimen ken at this time revealed no evidence tuberculosis on subsequent examination.

"At the time of this admission, there as no mention of a lesion in the left antecubital fossa, but the patient later stated that on the day following her injection she had noticed swelling, redness, and tenderness at the injection site. She had squeezed a small amount of serum from the lesion and had seen tubercle bacilli in a smear of this material.

"After eight days of study, the patient was discharged. On the following day, nine days after the injection, she again began to have severe chills and fever. She was readmitted on the fifteenth day after the injection with a temperature of 104° F. At this time she admitted for the first time that she had injected herself with tubercle bacilli. Considerable skepticism met this confession, however, and therapy was delayed for six days until a more positive diagnosis could be made. Physical examination was essentially negative except for a small, 1 mm. raised, slightly tender area in the left antecubital fossa. There was no enlargement of the left epitrochlear or axillary lymph nodes. The total erythrocyte and leukocyte counts and examinations of the urine revealed no abnormalities. Serum agglutination reactions for typhoid, paratyphoid, brucellosis, and typhus were negative and no malarial parasites were seen on examination of the blood. The erythrocyte sedimentation rate was 56 mm. in one hour.

"A chest roentgenogram obtained January 31, 1948 revealed no abnormalities after six days of a bounding fever with daily spikes up to 104° F. Streptomycin therapy (3.0 Gm. daily by the intramuscular route) was instituted because of the appearance of a generalized miliary infiltration throughout both lungs. . . . The infiltration had appeared at some time between the sixteenth and twenty-first days after the inoculation with tubercle bacilli. At this time (February 4) large numbers of acid-fast bacilli were seen on examination of a smear prepared from a small amount of serum expressed from the lesion in the left antecubital fossa. Cultures (Dubos, Petragnani) of this material were subsequently positive for *M. tuberculosis*. A tuberculin skin test with 1:100,000 dilution O. T., performed on February 5, was negative after 48 hours' observation.

"Repeated blood cultures on both Petragnani and Dubos mediums obtained after the start of streptomycin therapy

were sterile. Moreover, subsequent guinea pig inoculation of the patient's blood, urine, and cerebrospinal fluid yielded negative results. The cerebrospinal fluid sugar, protein, chlorides, gold curve, and microscopic examination remained normal throughout the patient's hospital stay. Frequent microscopic examinations of the urine over a period of three months showed no abnormalities. The total leukocyte and differential counts remained within normal limits, whereas the patient showed a mild hypochromic, microcytic anemia one month after the beginning of her illness. This was subsequently corrected with the help of one 500 cc. whole blood transfusion, the administration of iron sulfate, and control of her infection.

"The only areas manifestly affected by this massive injection of tubercle bacilli were the site of the injection and the lungs. The tip of the spleen was barely palpable on one occasion eight days after admission to the hospital during the height of the fever. Subsequent examinations, however, revealed no consistently demonstrable splenic enlargement. The ocular fundi showed no abnormalities at any time. Sputum examinations for tubercle bacilli were negative on two occasions. A tuberculin skin test, 1:10,000, was positive after 48 hours on the twenty-sixth day after the inoculation. No significance was attached to this positive reaction because of the history of a previously positive tuberculin skin test in 1946.

"It is probable that the immunity provided by the infection prior to 1946 was minimal in the presence of so great a dose of injected tubercle bacilli. The lungs had apparently filtered out the majority of injected bacteria, thus preventing, with the help of streptomycin therapy, hematogenous spread to the other organs of the body.

"There were available as indexes of the success of streptomycin therapy the chest roentgenograms, determinations of the erythrocyte sedimentation rate and temperature readings, the local abscess at the site of injection, and the patient's subjective improvement. She remained on the original dose of streptomycin (3.0 Gm. daily) for 19 days with little or no definite improvement in the symptoms of general malaise, headaches, and shaking chills. Her temperature remained elevated with daily spikes to 103° to 104° F. During time (February 19) a chest roentgenog showed that the miliary lesions in lungs were more sharply circumscribed increased in number. The lesion in her antecubital fossa had not improved s the initiation of therapy. In the belief t larger doses of streptomycin might con the infection, the dose was increased 5.0 Gm. a day and continued for four d without apparent improvement. The d was then reduced to 2.0 Gm. of strepto cin per day because of the lack of impro ment and severe vertigo.

"At this time (February 23) the pati began to complain of a rather severe p in the area of the venipuncture. Wet dr ings were applied to the site of the inj tion and these seemed to give relief. the following day, the puncture wou opened and considerable thick, yellow pus was discharged. Following this, patient's temperature dropped to 100° and remained there for seven days a then fell to 99° F.

"From the twenty-third day of thera the patient's feeling of well-being improv dramatically. A roentgenogram of the ch taken on the thirty-eighth day of thera (March 6, 1948) showed the lesions in t lungs to be static and the lesion on the l arm was definitely improved.

"From the thirtieth day of therapy, t patient's temperature remained norm and a chest roentgenogram on the sixt fifth day of treatment showed definite i provement in the lung lesions. At this ti (April 8, 1948) the lesion on the left a had completely healed, and the patie had no symptoms except for moderate d ziness from the streptomycin therapy. N auditory changes were observed in ser audiograms.

"One of the most fortunate factors ai ing the recovery of this patient was t fact that the tubercle bacilli initially cu tured from the lesion in the left ant cubital fossa (Dubos medium) show sensitivity to a concentration of less th 1.0 γ of streptomycin per cc.

"The patient received a total of 241 Gm. of streptomycin over a period of 1 days. She was discharged to her home her one hundred and twenty-fifth hospit day with no recurrence of symptoms fo lowing cessation of therapy. Her last roen

gram obtained three weeks before dis-ge (May 7, 1948) showed the lesions ie lungs to be less intense and more ly circumscribed than on previous inations. The erythrocyte sedimen-n rate at the time of discharge was m. in one hour.

his patient has been carefully follow-nd a report from her physician in 1948 stated that she was exercising rately, felt well, and had gained ht. A chest film, July 26, 1948, re-d no abnormalities whatsoever.

letter received in October from this fortunate young lady stated she had working since September in a blood in the hospital of her home town. also stated that her health was fine confirmed this statement by the news r marriage in early September 1948."

romycetin in the Successful Treat-ent of Recurring Epididymitis — EDEWILL, F. H. — *Journal of Urology*, 2: 581 (October) 1949.

pididymitis strikes out of a clear sky. literature is full of traumatic types ucing epididymitis, nonspecific too, with urethra normal." One writer s: " 'There is a type of patient, usual-etween 30 and 50 years of age, who gone to a private physician for his state gland" being treated with a series ilatations, sounds, massages and fre-tly some form of instillations. The toms of these patients vary, but the common complaints are of a drawing pain in their rectum, perineum, or s penis, backache, pain in the groin, or leg, sexual asthenia, functional im-nce, hemospermia, premature or in-ntary ejaculations, sometimes associ-with pain in the joints etc., with more ss typical symptoms of chronic pos-r urethritis. Usually the patient asks is ever going to get well. If a quick ination is made, a diagnosis of chronic tatitis or posterior urethritis is prob-meaning more sounds and massages administration of a sulfa drug. If such tient fails to improve he may either lischarged or passed along to a psy-trist who, in turn, may find him neu-'

"However, urologists by routine rectal examination in many cases with palpation, massage, and study of expressed secretion can determine the extent of seminal vesicle as well as prostate involvement." But one runs across cases all of the time in which such examinations reveal nothing. "In many cases the seminal vesicles are not examined at all."

The literature is replete with cases of routinely treated prostates with indications of recurring symptoms and absorption pointing to the seminal vesicles as the site of focal infection. And with protracted treatment, in such a case neurasthenia may develop. Yet why, when men are considered in perfect health like the cases reported by several writers, one lifting one end of a piano, the other slipping on a rug and attempted with sudden muscular effort to prevent falling, why do they both develop acute epididymitis? Given a low grade, unsurmised infection of the seminal vesicles and ducts as well as a condition simulating a cord bladder, and one has the answer. "With a sudden so-called 'strain' placing as much as 50 pounds' extra pressure on the partially filled bladder with the internal sphincter giving way, and external sphincter still in a spastic state, the transmitted hydraulic pressure forces urine into the ejaculatory duct, passing through the ampulla on down to the globus minor, the urine carrying with it infection from pathological changes above. Why does the urine pass into only one duct in 90 per cent of the cases? Because, as discovered by those who have attempted to catheterize chronically infected ducts, the patency is very seldom the same in the two ducts; i.e., one duct is patent, the other usually not. . . . So the urine, if not infected before, becomes infected on its way and quickly produces epididymitis on one side."

One of the problems that interests the writer is can chloromycetin check the epididymitis that may follow prostatectomy? Several writers have routinely performed vasectomy before removing the prostate to prevent attacks of epididymitis, that occur in 15 per cent of all cases when vasectomy is not done. Even with vasectomy 4 per cent of the cases develop epididymitis anyway. With chloromycetin, using, say 3 Gm. as an initial dose, there

is a constant excretion of 80 millimicrons for over 24 hours; then with a maintenance dose of 1/4 Gm. by mouth every 3 hours, whether one has a retention catheter or drainage tubes, this drug used preoperatively and postoperatively should prepare the patient for such an eventuality. "Implementing penicillin to take care of gram-positive coccci together with chloromycetin to keep the tract clear of all other of the commoner pathological bacteria, and with no danger of fastness developing, even with catheters and drainage tubes present, it is quite possible such use of these drugs will eliminate the necessity of vasectomy before prostatectomy is performed."

"Cases are reported in which acute epididymitis cleared up in a remarkably short time with chloromycetin."

"Case 1.—R. A., aged 35, 5 feet 8 inches, weight 152 pounds, had never been sick in his life, had mumps of the left testicle with parotiditis on both sides of the face. The temperature was 103.5° F. The condition of testicle was most troublesome. Using 60 mg. chloromycetin per kilo of body weight, about 4 Gm. initial dose, broken into 4 capsules each hour for 4 hours, and then 1 capsule was given every 3 hours. In 12 hours all pain left the testicle, and in 20 hours after starting chloromycetin the patient became afebrile. In 26 hours after starting chloromycetin no symptoms or signs existed in the neck or scrotum. He became ambulatory the third day after treatment.

"Case 2.—C. W., white, aged 38, height 5 feet 11 inches, weight 175 pounds, had had gonorrhea 12 years previously, followed by recurring epididymitis." He came to the writer with the fifth attack of epididymitis in two years, and he claimed that the epididymitis followed a "strain." "The history of each attack was about the same. While doing heavy lifting with the bladder partly filled with urine he would suddenly develop a sharp stabbing pain in the left testicle followed by epididymitis that would remain painful and swollen for two weeks. Except for the attacks of epididymitis that were crippling and frightfully painful, the patient had always been well. Examination showed swelling and tenderness in the left side of scrotum involving the epididymis. The temperature was 101.5 F. The attack of epididymitis started the day before admission. The urine sho coli, Friedländer and Proteus." The w gave him 1 Gm. chloromycetin every for 4 hours and then 1/2 Gm. eve hours by mouth. "In 36 hours all pain appeared and swelling was reduced one half. In 48 hours all swelling had appeared."

Case 3.—A. R. aged 44, white, he 5 feet 9 inches, 160 pounds weight, been treated by the writer twice be for similar attacks. "His attack al seemed to follow a 'strain' of heavy lif Examination between attacks reveale coccal and staphylococcal infection of seminal vesicles and prostate. Besides tine treatment he was put on sulfa d and penicillin, but he did not cont treatment long enough to become c between attacks." At his last attack, ruary 4, 1949, the writer examined posterior urethra during and after the attack. "He was given 4 Gm. of chl mycetin in broken doses and 1/4 thereafter every 3 hours by mouth. Ne he nor any of the other patients sho any toxic effect from the drug." Becaus had *Staphylococcus aureus* infection well, the writer gave him procaine pen lin 300,000 units intramuscularly d Chloromycetin is 10 times weaker penicillin against that particular coccu the writer used the synergistic action of two drugs. "He had no pain the next became afebrile and the swelling disapp ed in two days. The two drugs were tinued seven days longer. Then the se tion from the seminal vesicles and u was free of any bacteria.

"Case 4.—E. H. K., aged 25, heig feet 10 inches, weight 153 pounds, ha neisserian infection four years previous During the last two years he had t attacks of epididymitis on the left side reported to the writer the last time January 14, 1949. After the attack year ago, on urethroscopic examination injection of the left ejaculatory duct diodrast, the writer found it patent to globus minor, and a dilated seminal ves that filled poorly. "Streptomycin and s adiazine were given for the attack at time. He did not continue treatment enough to clear up his infection last y On January 14, 1949 organisms pre were gonococci and coli."

n January 13 the patient was lifting heavy pipe for a construction com- and suddenly a severe pain was felt s left scrotal sac. On January 14 the dymis was very large and painful. temperature was 102.5° F. He was d on 3 Gm. chloromycetin and the Gm. every 3 hours. During this attack urine and slides showed gonococci and bacilli. The infection cleared up on chloromycetin in 50 hours, and drug was continued for 10 days. Final ination revealed no bacilluria and nor- seminal vesicles and prostate. It is ely that the patient will have any so-called 'strain.'

Case 5.—R. F., aged 52, height 5 feet, ches, weight 200, had a hypertrophied ate grade 1. No residual urine was d; he had had three attacks of epi- mitis from a 'strain' during the past months. He had gonorrhea 15 years nd again 3 years ago. He had posterior ral strictures necessitating the pas- of sounds. He refused further treat- and harbored *B. coli* and Proteus in urine. His last attack of epididymitis March 30, 1949 following what he d a 'strain' in the left epididymis. He a chronic low grade infection of the nal vesicles and ducts. Chloromycetin ed up the attack in 60 hours, whereas rmer attacks he had suffered for 16 . He was on the drug one week follow- recovery. Two weeks later his urine was le."

Factors Promoting Erythropoiesis. ignificance and Applications — ONI, P. — *La Diagnosi*, 5: 341 (Sep- mber) 1949.

mmediately after discovery of the apeutic effect of liver in pernicious ia the hypothesis was advanced that icious anemia might be a deficiency ase but all attempts to isolate and tify the active factor in liver were un- essful. The problem was made more plicated by experiments which demon- ted that at least two factors intervene he pathogenesis of pernicious anemia, extrinsic factor present in some foods the intrinsic factor present in normal an gastric juice but absent in that of ents with pernicious anemia; the interaction of these two factors would lead to the hematopoietic principle present in liver and liver extracts. Lack of the intrinsic factor would then be the supposed cause of true pernicious anemia, while in other macrocytic anemias a deficiency of the extrinsic factor might be dealt with. None of the various vitamins could be identified with the extrinsic or intrinsic factor, but a close relationship had to be assumed between the vitamins of the B group and the antipernicious factors, as the liver is a rich source of vitamin B and as on the other hand yeast concentrates which are also rich in vitamin B have a definitely favorable effect in pernicious anemia, and particularly in other macrocytic anemic syndromes. On the basis of the discovery that a certain number of substances, probably linked to the vitamins of the B group, are necessary for the development of certain microorganisms and with the availability of adequate procedures of chemicomicrobiologic research identification and synthesis of a chemically pure substance was achieved; namely, folic acid or pteroyl-glutamic acid, which had a pronounced curative effect in pernicious anemia and in other related syndromes. The pteroyl-glutamic acid is a compound of pteridine, paraamino benzoic acid and glutamic acid, and some factors described under different names are probably mostly conjugates of folic acid, differing by the number of molecules of glutamic acid. In higher animals folic acid deficiency is characterized by hyperchromic macrocytic anemia, megaloblastic hyperplasia of the bone marrow and leukopenia.

While folic acid produces a beneficial effect in pernicious anemia it is not identical with the antipernicious factor of the liver, as it is present in only minute quantities even in the most highly concentrated and active liver extracts, does not induce remissions of the nervous symptoms and the glossitis associated with true pernicious anemia, and is effective in macrocytic anemia of pregnancy in which liver extracts are not as effective. Folic acid is not identical with either the intrinsic or the extrinsic factor.

An interesting hypothesis states that paraamino benzoic acid is a precursor of folic acid and that the latter forms part

of an enzymatic system for the biologic synthesis of thymine or the conversion of the latter into a precursor of nucleic acid. Large doses of thymine have a favorable effect on macrocytic anemias.

Repeated attempts to identify and isolate the antipernicious factor of the liver led to the discovery of vitamin B_{12} in March 1948; the difficulty of this work is illustrated by the fact that from a ton of fresh liver only 250 mg. of vitamin B_{12} are obtained. Vitamin B_{12} is a crystalline substance of red color, containing 4 per cent of cobalt; it is thermostabile and is inactivated at room temperature by solutions of sodium hydroxide and hydrochloric acid. Recently it has been found that vitamin B_{12} can be extracted from mediums on which *Streptomyces griseus* was cultured.

A single intramuscular injection of 6 to 15 gamma of vitamin B_{12} produces a good clinical and hematologic response in patients with true pernicious anemia, including improvement of the nervous symptoms and the glossitis. A single dose of 25 gamma produces complete restoration of normoblastosis within two days. One gamma of vitamin B_{12} is considered equivalent to one antianemic unit U.S.P.

In other macrocytic anemias, including those of pellagra and sprue, vitamin B_{12} seems as effective as liver extracts, but contrary to folic acid it seems little active in the macrocytic anemia of pregnancy.

Work has been done on the relations between vitamin B_{12} and the erythrocyte maturation factors; it has been shown that vitamin B_{12} is active perorally but requires much larger dosage in this case. However, if it is made to react with normal gastric juice before ingestion its effect is greatly potentialized and doses which were inadequate before will produce an optimal reticulocytic response. In the light of these experiments it seems likely that vitamin B_{12} represents the extrinsic factor and that the intrinsic factor is represented by one or more substances which are present in the gastric juice and capable of making vitamin B_{12} better assimilable. Furthermore as vitamin B_{12} is effective parenterally it may possibly be identified with the maturation factor of the erythrocytes. The primary alteration in pernicious a mia would consist in the lack of someth in the gastric secretion which makes vi min B_{12} easier to assimilate and utili

The significance and function of fi acid remains obscure. The most likely pothesis seems to be that folic acid is some manner liberated or activated vitamin B_{12} and constitutes the substa more immediately responsible for matu tion of the erythrocytes. In this case vitamin B_{12} would have to act directly through formation of other substances nervous system and mucous membra with respect to which folic acid is ineff tive.

Maturation of the erythrocytes wo be promoted in the following three m stages:

1. Mobilization of folic acid by vitan B_{12}.
2. Mobilization of thymine by folic ac
3. Utilization of thymine by the c of the red series.

Folic acid cannot be considered as dispensable in the nutrition of higher a mals but rather as a substance with spec pharmacologic effects. Practically in vi of the similarity of its therapeutic acti with that of liver extracts and of its hi cost vitamin B_{12} should be reserved cases with absolute hypersensitivity liver extract but this limitation does n diminish the physiopathologic importan of these new acquisitions.

Symptoms Attributable to Cold Hema glutination. Report of 2 Cases - BATEMAN, JEANNE C. — *Archives Internal Medicine*, 84: 523 (Octob 1949.

"Agglutination of all types of red blo cells at cold temperatures by serum, w reversal at warm temperatures, occurs a wide variety of conditions. Cold hem glutination appears to be transient in ac infectious diseases, in trypanosomiasis, acute hemolytic anemia and in some ca of acquired chronic hemolytic anemia, possibly permanent in cirrhosis of the liv in Raynaud's syndrome (acrogangre and in some cases of acquired chro hemolytic anemia.

"The presence of cold hemagglutin is suspected when there is difficulty

d-counting procedures or cross match-
of blood at room temperatures, or the
lopment of acrocyanosis and hemo-
inuria are noted following exposure to
. Gangrene of a part may develop if
sure is prolonged. Less commonly,
mbotic phenomena are manifest."

Data in cases in the literature present-
the symptoms of cold hemagglutinins
been compiled. . . . These symptoms
ude acrocyanosis, thrombotic phenom-
hemoglobinuria and/or hemolytic
nia. They may occur separately but
frequently associated. Possible contrib-
g factors are sulfonamide therapy and
ilis."

The majority of cases occur in the
d, fourth and fifth decades, with the
test incidence in the fourth. The great-
ncidence in males than in females may
partly due to more frequent exposure
old, with consequent greater likelihood
development of symptoms. A great
ance exists in reported titer."

Case 1 is an example of vascular oc-
ion occurring in a case of primary
pical pneumonia accompanied with an
ated cold hemagglutinin titer.

Case 1.—N. O., a bartender of 22,
admitted on November 21, 1945 to
Third Medical Division of Bellevue
pital with complaints of a chilly feel-
fever, malaise, increasingly severe
oductive cough and dyspnea. There
moist rhonchi and fine rales in both
fields. Cultures of the blood and spu-
were negative. The white blood cell
t was 6,500. On November 25, penicil-
herapy was begun and the patient was
ed in an oxygen tent. Within 12 hours,
s and symptoms of thrombophlebitis
eloped in the superficial veins of the
t leg. It was noted that the oxygen
was unusually chilly. The patient
lually recovered. At no time did he
ive sulfonamide therapy. The cold
agglutinin titers were 1:1,280 on
ember 27, 1:2,560 on December 2
1:640 on January 10, 1946.

The most curious cases are those in
h transient or persistent high titers
old hemagglutinins suddenly develop
no apparent cause. Case 2 is an ex-
le.

Case 2.—M. L., an antique shop pro-
tor of 43, first experienced purplish blue mottling of the face, ears and fingers after exposure to cold in November 1944. The symptoms were followed by the passage of red urine. The patient's condition was diagnosed as 'kidney disease,' and he was treated with bed rest for two months. The symptoms reappeared when the patient was permitted to go out of doors but subsided during the following summer, only to reappear with the onset of cold weather. No jaundice was noted. There was no history of primary atypical pneumonia or of other viral infection. Physical examination was essentially noncontributory, except for acrocyanosis following exposure to the cold."

The patient was seen in the spring of 1946 by a physician who suspected the presence of cold hemagglutinins and referred him to the writer for further study.

"On April 19, the patient's cold hemagglutination titer, as determined by Kettel's method, was 1:2,621,440 against both his own erythrocytes and type 0 red blood cells. Gross clumping was noted in a specimen of oxalated blood obtained at room temperature. The red cells remained clumped after being removed from the refrigerator and standing at room temperature (23 C.) for four hours. Dispersion of erythrocytes took place at incubator temperature.

"The patient has been followed at the time of this report for a period of more than two years, during which he has remained in relatively good health. However, with exposure to cool weather there immediately develops bluish purple mottling of the ears, the cheeks, the tip of the nose and the fingers, accompanied with a mild sensation of tingling. About 15 minutes later, red urine is passed.

"The patient was urged to spend his winters in Florida, but this proved impractical; instead, he has consistently protected himself with warm gloves, stockings, etc., during cold weather."

Determinations of cold agglutination titer were made at intervals during the two year period. "There has been a wave-like decline in titer with a tendency for the titer to be lowest during the summer. However, the thermal range remains so wide that blood counts are possible only when warm pipets and diluting fluid are

used. A mild hypochromic anemia has developed.

"On February 10, 1948, salicylate therapy (5.2 Gm. of sodium salicylate daily in divided doses) was begun with the hope of blocking antigen-antibody reaction. At this time the cold agglutinin titer was 1:20,480. On February 17, it was 1:10,240 and the plasma salicylate level was 24.8 mg. per hundred cubic centimeters, as determined by the method of Brodie, Udenfriend and Coburn. The patient continued to show symptoms of acrocyanosis for several days after the institution of therapy. Subsidence was difficult to evaluate because of a sudden spell of warm weather. Side effects of malaise, ringing in the ears, anorexia and constipation were pronounced. The dose of sodium salicylate was reduced to 3.6 Gm.

"On February 24, the cold agglutinin titer had dropped to 1:2,560; the plasma salicylate level was 23.0 mg. Symptoms of anorexia, malaise and constipation persisted in a milder form.

"On March 2, the cold agglutinin titer was 1:20,480. Clumping persisted for two hours at room temperature (25 C.) up to a dilution of 1:1,280. The plasma salicylate level was 17 mg. Since the improvement suggested earlier had not been maintained it was decided to abandon the use of the drug.

"Subsequently the cold agglutinin titer fell spontaneously in a manner similar to that noted during previous summers."

"It is apparent that the primary mechanism responsible for symptoms due to the presence of cold hemagglutinins is intravascular clumping of erythrocytes. The precipitating factor is presumably cold, whether due to chilling in an oxygen tent, low outdoor temperature or, possibly, transfusion with chilled blood. Stasis then occurs, most apparent in peripheral parts of the body. Patchy cyanosis appears but usually subsides when the patient is exposed to a warm temperature. However, by then the tightly clumped erythrocytes have become more fragile than normal and tend to undergo hemolysis when subject to the trauma of circulation. Continued exposure to cold may cause the clumped erythrocytes to impede tissue oxygenation to the point where gangrene will develop in an extremity. This possibility should be considered in cases of bilateral gang in which exposure to cold alone has been of a degree severe enough to pro this pathologic process. Local throm of a deep part is more difficult to exp The primary mechanism is probably same. However, before erythrocyte dis sion can take place conversion of clumped erythrocytes into actual thro has taken place with all the known eff of vascular occlusion.

"Anemia of either of two types occur. There may be moderate chr anemia, such as the patient in cas exhibited. A probable explanation of disorder is that repeated bouts of hemol are severe enough to raise the hemoglo content of the blood to a level above renal threshold. The blood-forming ments, mainly iron, are then lost to body, and one may expect essentially iron-deficiency anemia which when unc plicated results in a hypochromic mi cytic blood picture. However, owing the difficulty in making correct bl counts and hematocrit determinations the presence of potent hemagglutinins is difficult or impossible to evaluate character of the anemia present. Occasi ally a hemolytic crisis takes place wit resultant severe anemia. Presumably, s den severe chilling could initiate such process, but such a history is rarely, ever, noted.

"Hemoglobinuria results whenever tu lar absorption falls behind filtration r The red color of the urine voided by th patients is due to the presence of hemog bin and not to that of free red blood ce

"It is a curious fact that the agglutin tion titer is not directly related to the t or degree of symptoms. Thermal range doubtless important, especially in low ti serums.

"Only a few cases with extremely hi titers of cold hemagglutinins have be reported."

"The effect of salicylates on the c hemagglutinin titer in the patient in c 2 was negligible. Two explanations suggested by the experimental studies other writers: First, the salicylates w given long after the beginning of antibo formation. Second, the action of salicyla is presumably less effective in the equiv lence zone in the region where antibod are in excess."

bacute Bacterial Endocarditis Due to Salmonella Typhimurium — DE SWIET, J. — *British Medical Journal*, 2: 1155 (November 19) 1949.

n view of the rarity of subacute bac- al endocarditis due to *Salmonella typhi- rium*, the following case is reported.

'A single girl, aged 19, a bottler in a neral water factory, was admitted to pital on June 1. There was no previous tory of illness of any kind apart from e fits in infancy. The present illness l started seven weeks before with gen- l weakness, occasional rigors, and epi- xis, and during the week preceding ad- ssion there had been unproductive cough l bouts of diarrhoea.

'On examination there were marked lor, furred tongue, sordes on the teeth, stration, and mental depression; tem- ature 103° F., pulse 112, respirations ; throat clear; pupils and fundi normal; neck rigidity or Kernig's sign; abdomi- reflexes absent, but all deep reflexes sent. A few scattered rhonchi were rd in the lungs. Examination showed enlargement of the heart clinically, but re was a marked gallop rhythm and a wing apical systolic murmur not con- ted into the axilla and not accompanied a thrill. The abdomen was slightly dis- ded and tumid on palpation, but the r and spleen were not felt. B.P. 120/80. hest radiograph on admission was clear. r white cells numbered 13,800 (80 per t polymorphs) and red cells 4,510,000 r c.mm.; Hb 81 per cent. Blood was t for culture and agglutination, and cimens of stool and urine for culture."

Her condition remained serious and her nperature continued without intermis- n; penicillin, 100,000 units three hourly, s started on June 3 and increased next y to 150,000 units three hourly without y effect. "On June 3 it was reported t there were no agglutinations to *Sal- nella typhi* O, *Salmonella typhi* H, *Sal- nella paratyphi B* O, *Salmonella para- phi B* H, nonspecific Salmonella H, or *ucella abortus*, but on June 6 *S. typhi- rium* had been cultured from the Widal t. In the meantime petechiae had ap- ared on the upper arms and at the root the neck, and her general condition had teriorated still further. The diagnosis s now apparently septicaemia due to *S. typhimurium* (subacute bacterial endocarditis), and it was decided to try to obtain a supply of chloramphenicol ('chloromycetin'). . . . Streptomycin was given six hourly in 1 Gm. doses. The chloramphenicol arrived after a total of 8 Gm. of streptomycin had been given, and by then the patient's general condition was decidely better, with fewer fresh petechiae and improvement in the gallop rhythm, but no marked fall in temperature. Sensitivity of the organism was demonstrated to chloramphenicol and to a greater degree to streptomycin.

"Chloramphenicol 4 Gm. (16 capsules of 0.25 Gm.) was given at 10 A.M. on June 8 and was continued in 1.5 Gm. doses twice daily; by 10 P.M. her temperature was normal. The next day the improvement in her toxaemia was quite marked, but she developed sudden pain and swelling in the right knee with severe limitation of movement. Fundus examination showed severe toxic changes in the right macular region, and a small subhyaloid haemorrhage in the left macular region. Her diarrhoea rapidly improved and was replaced by complete constipation; but fresh petechiae continued to appear, and in view of a slight rise in temperature on June 12 and 13 it was decided to double the dose of chloramphenicol by giving 1.5 Gm. six hourly. From then on her temperature did not rise above normal until she died. She continued to be extremely irritable and prostrated, however, and fresh petechiae appeared, though fewer in number; the blood pressure fell progressively to 66/50; the apical systolic murmur changed suddenly to a high-pitched musical murmur, and in spite of increasing the dosage again to 1.5 Gm. three hourly she developed acute pulmonary oedema and died on June 22. At no time were specific agglutinins demonstrated against this strain of *S. typhimurium*, and all specimens of stools and urine were negative on culture for that organism throughout.

"Postmortem examination showed no abnormality in the nervous system or in the abdomen, and in particular there were no lesions in the intestines, but two small white infarcts were found in the spleen. The lungs were very oedematous and there were a few small subpleural infarcts. The heart was normal in size but extremely

flabby, and the myocardium was very toxic in appearance and necrotic in parts. There were two vegetations on the mitral valve, one small and one moderate in size, and apparently still active but sterile on culture. Microscopy of the vegetations showed only polymorphs present in the fibrin, and no bacteria were seen."

Streptomycin in the Treatment of Subacute Bacterial Endocarditis — WALLACH, ROBERT AND POMERANTZ, NORMAN — *New England Journal of Medicine*, 241: 690 (November 3) 1949.

"A case of subacute bacterial endocarditis caused by Bacteroides and successfully treated with streptomycin is reported."

"P. R., a 53 year old waiter, was admitted to the New York Polyclinic Medical School and Hospital on December 2, 1947, because of increasing fatigue of six months' duration. Except for an occasional sore throat or pain in the knees he had been well until the previous July, when his remaining upper teeth had been extracted for replacement by a denture. Shortly after this he noticed increasing fatigue and weakness. Three weeks before admission he started to have fever, night sweats and chilly sensations; however, he continued to work. One week before admission he was forced to discontinue work because of weakness. He received seven daily injections of 300,000 units of penicillin in oil and wax without any appreciable effect on the fever, fatigue or night sweats.

"Although he does not remember ever having had rheumatic fever, he knew that he had 'murmurs of the heart' since childhood. He had had malaria at the age of 12, a tonsillectomy at 49 and a submucous resection at 51 years of age.

"Physical examination disclosed a well developed, fairly well nourished man of asthenic habitus. He appeared acutely ill. Close scrutiny of the skin and mucous membranes revealed no petechiae. The eyes, ears, nose, mouth and throat were normal except for the presence of an upper denture. The lungs were clear. The heart was enlarged, and the rhythm regular, and presystolic and systolic murmurs were heard at the apex. The liver and spleen were not palpable. The extremities were normal.

"Examination of the blood showed a red cell count of 3,650,000, with a hemoglobin of 72 per cent, and a white cell count of 8,000, with 65 per cent neutrophils, 34 per cent lymphocytes and 1 per cent eosinophils. Urinalysis was normal except for a faint trace of albumin; the sediment contained no red blood cells. The sedimentation rate (Westergren method) was 30 mm. in one hour, and the icteric index was 10. Blood cultures taken on the second, third and ninth hospital days were negative. Urinalysis repeated on the twenty-ninth and thirty-first days demonstrated no red blood cells in the sediment. A roentgenogram of the chest showed emphysema of the lungs and a globular-shaped heart whose borders extended to the right and the left."

"On the third hospital day two petechiae were found on the left buccal mucous membrane. On the fifth day penicillin, 500,000 units daily in divided doses every three hours, was begun. During the next 11 days the swinging temperature, night sweats and fatigue remained unchanged. New petechiae were found on 3 occasions, whereas the older ones faded. All were on the buccal mucosa. On the sixteenth day penicillin was increased to 800,000 units daily. For a few days the patient felt better and his appetite improved, but then he lapsed back to his previous state. On the twenty-fifth day the penicillin was increased to 2,400,000 units daily. On the next day two new petechiae appeared in the right conjunctiva, and one on the lower lip. Because it was believed that he was not making any progress, penicillin was discontinued on the twenty-eighth day.

"Blood cultures were taken on the thirty-second, thirty-third and thirty-fourth days. After all therapy had been stopped the daily temperature spikes reached higher levels, and his general condition seemed to deteriorate more rapidly. On the thirty-seventh day it was believed that further delay might cause irreparable damage, and penicillin therapy was resumed, massive doses (5,000,000 units daily) being used. Although the temperature fell somewhat he remained otherwise unchanged and on the forty-first day new petechiae appeared in the left conjunctiva. On the forty-

nd day the blood culture taken on thirty-second day was reported positive for bacteroids. Streptomycin, 4 Gm. y in divided doses every three hours, then started and continued for 28 s. Four days later, on the forty-sixth , the penicillin was discontinued. From forty-fifth day (three days after the t of streptomycin therapy) clinical improvement was marked. His appetite improved, and he became more alert. From forty-ninth day the temperature remained below 100° F. No new petechiae eared after streptomycin had been ted. Two blood cultures taken after beginning of streptomycin therapy ty-seventh and fifty-third days) and after its termination (sixty-ninth and nty-sixth days) were negative. During third week of therapy symptoms of ptomycin toxicity appeared. The patient complained of dizziness, but his hearing remained unimpaired. The dizziness sisted for six months. When last seen May, 1949, 14 months after discharge, was in excellent health and working although he still had a slight gait disturbance."

Note on the Dosage of Quinine To Be Administered in Acute Malaria—VINCKEL, Ch. W. F. — *Revue du Paludisme et de médecine tropicale*, 7: 239 (November 15) 1949.

It is understandable that in a country re the malignant strains of *Plasmodium iparum* predominate there is a tendency increase the daily dose of quinine as pared to that in countries where only benign *Plasmodium vivax* is encountered which responds readily and rapidly to tment, and also that smaller doses are uired in small people like the Annamese n in big white races or black races. wever, the literature on quinine dosage udes marked differences of opinion ch cannot be related to these factors. he necessity of a local determination of optimal daily dosage of quinine has n shown clearly; in 19 cases of infection with one of the Indian strains of *P. iparum* it was demonstrated that average dose of 40 grains is sufficient for cure of a primary attack and the complete treatment amounted to 117 grains, while in 13 cases of infection with Rumanian or Sardinian strains of *P. falciparum* doses of 335 and 1,680 grains respectively were required, indicating the enormous differences. However, the importance of this study on a small number of cases should not be overestimated.

The author tabulates the doses recommended in various books and articles and concludes from the list that a daily dose of between 0.5 and 2.5 Gm. has been advised for adults; particularly in the United States recently very large doses have been recommended. These variations are in striking contrast to the fact that experimentally in avian malaria the required dosage can be determined with high accuracy. With increased dosage the subjective side effects like tinnitus, deafness and nausea increase and the same applies to the more serious consequences usually like temporary visual and auditory disturbances. Physicians who prescribe subtoxic doses forget that the goal of treatment is cure of the patient rather than poisoning of the parasites. One writer stresses that immunity and chemotherapeutic treatment must supplement each other in the cure of malaria and that early administration of high doses of quinine or other specifics interferes with the development of immunity.

With convenient doses of quinine many, but not all parasites are killed, and a certain amount of antigen comes in contact with the somatic cells, stimulating phagocytosis and formation of antibodies. When this defense mechanism becomes powerful enough the surviving parasites are killed in turn; some of the more resistant ones may survive but will be kept in check by the defense powers of the organism. Quinine produces an "immunizing shock" but the cells must be in a condition to respond properly and the drug must not be given in a dose which damages them. According to one writer doses of 4.0 Gm. or more are less effective than smaller ones, and observation was made of cases in which discontinuation of quinine treatment proved highly beneficial; at the expected time after discontinuation a relapse occurred but it was readily controlled by a moderate dose of quinine (1.0 Gm. per day). No explanation of the high

dosage recommended is to be found in the corresponding papers, and the Commission on Malaria of the old League of Nations, composed of the most eminent malariologists of various nations, had recommended a daily dosage of 1.0 to 1.3 Gm. It has been pointed out that even in benign *P. vivax* malaria the blood cannot be sterilized by simply increasing the dosage of quinine, and doses up to 5.5 to 7.5 Gm. have been used unsuccessfully in Liverpool. One demonstrated that 0.6 Gm. of quinine hydrochloride is sufficient for treatment of the acute attack. According to another the main effect of quinine is that of provoking the process of immunization and only a low dosage is required for this purpose while a high dosage exhausts the somatic cells charged with the production of antibodies.

Quinine is a general protoplasma poison. Experiments were made on 134 malaria patients, 94 with *P. vivax* and 40 with *P. falciparum* malaria. It was found that a dosage of 0.6 Gm. achieved as good if not better (more rapid) results as one of 1.2 Gm. and the dosage of 0.6 Gm. was given in all cases.

The author concludes with the hope that in the interest of suffering humanity the authorities will come to recommend the lower quinine dosages, with due consideration of the local particularities of the parasitic strains.

Streptomycin in the Treatment of Tuberculous Sinuses. Review of 11 Cases — DAVIS, R. HARVARD — *Lancet*, 2: 982 (November 26) 1949.

"Systemic streptomycin therapy has been given to 11 patients with 26 draining cutaneous tuberculous sinuses, which in 5 cases originated in bone and in 3 followed thoracoplasty, in 2 nephrectomy, and in 1 Monaldi drainage."

"The dosage of streptomycin adopted was usually 1 Gm. daily, but in some acute cases 0.75 Gm. was given twice daily; the total dose depended on the response, and no local treatment with streptomycin was attempted. In all the 8 proved tuberculous cases the tubercle bacillus was of the human type."

Therapeutic Effects.—General: One of the most conspicuous features in all the cases was the exceptional improvement i the patient's general condition, which v subsequently maintained; in 4 cases t response was such that, owing to the e treme sinus cachexia, streptomycin thera was a lifesaving measure. "The contr of the toxaemia was reflected in the te perature chart; in most cases the tempe ture settled within three or four weeks the start of treatment. An improved app tite was a notable feature of all cases, a the few patients who were weighed regul ly showed a definite increase of weig during and after treatment.

"Local: A favourable local response streptomycin was shown by the dischar from the sinus becoming serous instead purulent and diminishing in quantity. T occurred within three or four weeks of t start of streptomycin therapy and was f lowed by the development of healthy gra ulation tissue, a scab, and finally a fir healthy scar. . . . In the present series per cent of the sinuses healed within thr months; and a further 25 per cent aft three months; and the single sinus r maining open looks much healthier. N sinus has reopened. One required plast surgery owing to its size. The time take by the sinuses to close was as follows:

Analysis of Cases

Time taken	No. of sinus
One month	2 (7.1%
Six weeks	8 (28.6%
Two months	2 (7.1%
Three months	8 (28.6%
More than three months	7 (25 %
Remained open	1 (3.6%

"The average duration before treatme was about 11 1/2 months, and the averag length of time since closure is 3 months days, the longest being 7 months 15 day

"Other Lesions: No change was obser ed in pulmonary lesions, and only 1 ca of early joint tuberculosis showed a stri ing improvement.

"Complications: There was some di comfort at the site of injection in mo cases, but it was never severe." Thr cases had some transient giddiness in t first few weeks, but the dosage was n reduced, and no permanent vestibular dam age was apparent. One case had a mil urticarial rash on the face on the fiftie day, but it subsided rapidly when 'Ben

was given. "These complications were than had been expected from earlier rts and confirm the observation that, e dosage is kept below 2 Gm. daily, plications are considerably reduced."

siderations to the Problem of the ssociated Coronary and Cerebral yndrome — Fazio, Cornelio — *chweizerische medizinische Wochenchrift*, 79: 1108 (November 19) 1949.

ecently an increasing number of cases ransitory or permanent hemiplegia in tion to a myocardial infarction has n reported and these reports have re- ed in an interesting pathogenetic dis- sion. One writer divided the symptoms lamage to the nerve centers in relation myocardial infarction into two groups; hely, transitory generalized neurologic nomena like restlessness, anxiety, cold at, confusional conditions, and disturb- es of consciousness which to a modest ree are almost constantly present at time the syndrome of myocardial in- ction develops but which may subse- ntly assume the characteristics of the re complicated syndrome of the cerebral e of myocardial infarction and focal rologic symptoms, usually in the form a more or less complete hemiplegia ich may appear at the onset of the arction together with syncopal attacks, several hours to even days later.

The first reports considered only cer- al embolism from mobilization of parie- thrombi resulting from the myocardial arction as pathogenetic factor of the ociated coronary and cerebral syndrome, t it has been found that the embolic ory does not account for perhaps the st frequent cases in which the hemi- gia appears simultaneously with or rtly after the coronary thrombosis. It s then considered possible that the myo- rdial infarction may by sudden changes the hemodynamic conditions and in sociation with preexistent thrombogenic sions of the cerebral vessels produce cer- ral thrombosis in analogy to the coro- ry one. The myocardial infarction would en play the part of a provoking cause, t to be considered as specific in the sense a direct relationship between cardiac sion and cerebral apoplexy but as a dis- turbing factor of the cerebral circulation, manifesting itself particularly by a fall of the arterial pressure and a slowing down of the circulatory speed. The conception was advanced that not only myocardial infarction but other cardiac affections as well may predispose to strokes or provoke them in patients with altered cerebral vessels, corresponding to the state of heart failure. These recent conceptions are in agreement with present day knowledge concerning the pathogenesis of focal lesions of the cerebral vessels in general.

It becomes increasingly clear that cerebral apoplexy is a syndrome caused by local alterations of the cerebral circulation and that these alterations may depend on various complex factors with localization inside or outside the skull and of mechanical, chemical or nervous nature; any of these factors may be decisive or only conditioning in the individual case. It is then understandable that the syndrome is caused in some cases by local vascular lesions exclusively, including rupture, or obliteration of the vessel and functional alterations of the vascular area under consideration, while in others it represents the expression of simultaneous disturbances of the cerebral and systemic circulation, of an organic or functional nature. A circulation with perfect and uniform function will respond sufficiently to any extracerebral circulatory disturbance by means of its various compensatory mechanisms while a cerebral circulation which is limited in its functions by preexistent organic or functional alterations will not be able to cope with extraordinary demands. In this sense myocardial infarction, and cardiac affections in general, represent only one of the factors which may contribute to the origin of cerebral apoplexy; other factors possibly responsible for sudden circulatory disturbances include some types of arterial hypertension, renal affections with hyperazotemia, intense hemorrhages of the stomach or other organs, therapeutic venesections, altered reflex functions of the carotid sinus and others. These observations do not rule out the pathogenetic significance of local arterial and venous organic and functional pathologic factors in focal lesions of the cerebral vessels but only signify that local and extracerebral factors are united into an indivisible

entity, and that in some cases at least apoplexy is to be considered the cerebral manifestation of a systemic pathologic situation. It is interesting to note that both physiologically and anatomically there exists a close parallelism between hemorrhagic infarction of some thoracic and abdominal organs and certain syndromes of the cerebral vessels, and that circulatory disturbances in the thoracic and abdominal organs are frequently found on autopsy after cerebral apoplexy.

The author does not deny the possibility of cerebral malacia by embolism or primary thrombosis but stresses the necessity of limiting the terms of embolic or thrombotic apoplexy to cases with anatomic confirmation as malacia may be caused by a predominantly or even exclusively functional disturbance of the systemic or cerebral circulation without disturbance of the patency of the vessels on anatomic examination. Even on autopsy differentiation between embolic and thrombotic processes, and in the latter case determination whether the thrombosis is primary or secondary to slowing of the circulation on the basis of other causes is often very difficult.

The possibility that a focal lesion of the cerebral vessels even of a permanent nature may form independently of an embolic or primary thrombotic process affords a better understanding of the close pathogenetic and clinical relations between transitory apoplexy and apoplexy with permanent defects. The author does not agree with those who claim that transitory apoplexy is caused by functional circulatory disturbances like spasm, and permanent apoplexy by organic obstruction of the vessel by thrombus or embolus, but he believes that the same pathologic factors, probably depending on intensity or simultaneous action of other factors, may cause either a reversible circulatory disturbance which disrupts the cerebral function only transitorily, or a severer circulatory disturbance which results in irreversible parenchymatous alterations. More attention should be paid to the pathogenetic and anatomic criteria of differentiation between hemorrhage, ischemic malacia and hemorrhagic malacia and correlation to the neurologic syndrome.

The author finally stresses that th three types of cerebral lesions have dif ent anatomic characteristics and theref probably at least a partially differ pathogenesis. Future studies of the a ciated cardiac and cerebral syndrc should be made with a more accurate a tomicoclinical attitude and with the g of determination of the various cere and extracerebral functional and orga pathologic conditions which favor prod tion of the anatomically different ty of cerebral vascular lesions.

The Diagnostic Significance of "Bur Red Blood Cells — Schwartz, S ven O. and Motto, Salvatore A. *American Journal of the Medical S ences*, 128: 563 (November) 1949.

"In the course of the routine review blood films a peculiar red cell, measuri about 7.5 microns or less in diameter a having one or more large spiny projectio along its periphery, was seen from time time. The impression was gradually gain that this form represented an entity whic although occasionally encountered in oth conditions, occurred most frequently uremia, carcinoma of the stomach, a peptic ulcer with bleeding." The write have found that this peculiar poikilocyt which they have designated "burr" ce often offers the first clue to diagnosis. E perience has taught them to use "burr cells as valuable signposts in the etiologi evaluation of anemias. "This study was un dertaken to test the validity of what, t the present time, had been simply an im pression, and to determine the frequenc with which 'burr' cells occur in both nor mal and abnormal states."

"Blood films from 75 cases of uremia 50 cases of carcinoma of the stomach, an 50 cases of bleeding peptic ulcer wer studied. The control series was made up of two groups. The first consisted of 10 consecutive blood films obtained from pa tients entering the medical wards of the hospital for miscellaneous conditions an having no hematologic aberrations, while the second was made up of 100 similarly obtained bloods which showed some hema tologic abnormality such as anemia, leukocytosis, poikilocytosis, and so on.

"The diagnosis of uremia was made on the basis of azotemia together with one or

re of the clinical findings of nausea, niting, irritability, lethargy, uremic st, pericarditis, and coma. All patients l blood creatinine levels of 3 mg. per) cc. or over and nonprotein nitrogen els of 70 mg. per 100 cc. or more. Of 75 patients whose bloods were studied, died. The blood pressure was 150/90 over in 62 of these cases.

"The diagnoses of carcinoma of the mach and bleeding peptic ulcer were stantiated by gastroscopy, roentgen , and, or, surgery.

"One thousand red blood cells were nted on each dry blood film. In addi- n, 25 wet preparations were made; 15 m the blood of uremic patients, 5 from ients with carcinomas of the stomach, l 5 from patients with bleeding peptic ers, in order to study the appearance the cells in a relatively unmodified te."

The writers were particularly interested determining whether the "burr" cell s a form of poikilocyte or a crenated cell. he appearance and frequency of occur- ce of the 'burr' cell in the wet prepara- ns leave little doubt but that these ls represent a preformed poikilocyte and a crenated cell. There are occasional rr' cells, however, which are difficult to ferentiate from crenated cells.

"The 'burr' cell is a mature erythrocyte out 7.5 microns or less in diameter, ich has one to several spiny projections ng its periphery." The writers have sen to call it "burr" cell because of its emblance to the prickly envelope of a rr. " 'Burr' cells differ from crenated red ls in that the latter have many, fairly nmetrically arranged small spiny projec- ns which often occur on the surface as ll as the periphery; and whereas crenat- cells occur in groups, sometimes more one area than another, 'burr' cells are rly evenly scattered throughout the od film. In the enumeration of 'burr' ls for this study only those were counted ich were untouched by adjacent cells d which were located in fields in which crenated cells were present.

"Of the 75 cases of uremia, 54 cases wed 'burr' cells. The range of incidence the 'burr' cell in this group was 0.1 r cent to 1.5 per cent (1 to 15 'burr' ls per 1,000 red cells counted). No correlation existed between the incidence of 'burr' cells and race, sex, age, height of blood pressure, anemia, color index, or the levels of the nonprotein nitrogen or creatinine.

"Of the 50 patients with carcinoma of the stomach, 34 had 'burr' cells. The per cent incidence of the 'burr' cell in this group was from 0.1 to 3.7 (1 to 37 'burr' cells per 1,000 red blood cells counted). No correlation was demonstrable between the incidence of 'burr' cells and race, sex, age, and the anemia or the color index.

"Of the 50 patients with bleeding peptic ulcers, 27 showed 'burr' cells. The range of the incidence of 'burr' cells in this group was 0.1 per cent to 1.2 per cent (1 to 12 'burr' cells per 1,000 red cells counted). In this series there were 37 patients with duodenal ulcers, 11 with gastric ulcers, and 2 with marginal ulcers. No correlation existed between 'burr' cell incidence and the site of the ulcer, race, sex, age, anemia or the color index.

"On the 100 blood films of the control group which revealed miscellaneous nonhematologic diseases, no 'burr' cells were found; while in the 100 preparations obtained from patients showing some hematologic aberration, 21 had 'burr' cells." The 21 cases were made up of the following conditions:

Azotemia	8
Organic Heart Disease	1
Organic Heart Disease with Failure	2
Carcinoma—Rectum	2
Carcinoma—Gastrointestinal—site unknown	2
Carcinoma-stomach	1
Pernicious Anemia	1
Pernicious Anemia—with Carcinoma of Stomach	1
Malnutrition	1
Tuberculosis	1
Thyrotoxicosis	1

"This study failed to reveal the pathogenesis of the 'burr' red cell and did not elucidate the common denominators among uremia, carcinoma of the stomach, and bleeding peptic ulcer. Severity of anemia, level of color index, amount or duration of bleeding, degree of nitrogen retention, age, sex and race were all taken to be insignificant. Hypoproteinemia and blood in the intestinal tract may play a part." Dehydration is apparently not a significant factor, as the writers have not commonly observed "burr" cells in severely dehydrated diabetic patients in acidosis.

The Present State of Physiopathology and Treatment of Seasickness — San Antonio Alvarez, Joaquín — *Medicina*, 17: 223 (October) 1949.

Seasickness is an undefinable sensation of general malaise, followed by nausea and vomiting, and for its study a distinction between the patient's actual sensations and his interpretations is necessary; thus the patients speak of vertigo while subjective rotation and ocular nystagmus, characteristic of experimental vertigo, are absent. While no physiopathologic theory of seasickness has been generally accepted, that of the labyrinth is the most acceptable one. Children up to the age of 2 and people over 40 have a lesser predisposition, while a tendency to general nervosity or to restraint has no influence. According to one writer development of the knowledge of seasickness consists of the successive periods of description of the symptoms, investigation of its genesis and empirical treatment, the conception of vagotonia, and the conception of labyrinthine disturbances.

After a survey of the older theories the author points out that with respect to the theory of labyrinthine stimulation as the fundamental cause of seasickness one stressed that the form rather than the intensity of the movements is decisive. While in experimental vertigo the semicircular canals are chiefly involved, in seasickness utriculus and sacculus are the decisive factors as their movements act more intensely on the respective maculas due to the presence of its otoliths. The labyrinthine stimulation is carried through the vestibular nerve to its bulbar nuclei where connection with the brain and vegetative system is established leading to the well established clinical syndrome. However, in such a polymorphous process other factors are needed for explanation of the subjective symptoms at the onset of the process, and in this respect one may resort to the old theory of anemia of the cerebral and diencephalic centers, with generalized vasoconstriction possibly due to suprarenal discharge; this would account for pallor of the face, pollakiuria, headache and somnolence at the onset of the syndrome. The labyrinthine symptoms proper would then follow, and by contiguity with the bulbar connecting centers or directly th vagus nucleus would be stimulated, leadin to vagal vomiting and the other parasym pathetic symptoms like sialorrhea. Th syndrome is then complicated by the affec tive sphere and the special emotionalit of the individual, depending on macula hypersensitivity or hyposensitivity. On writer related all these processes to a com bined labyrinthine, vegetative, cortical an diencephalic action; another stressed th importance of an increase of the intra labyrinthine pressure, consecutive to in crease of the intracranial pressure and re lated to blood pressure and vasoconstric tion.

After a lengthy discussion of the anat omy and physiology of the eighth crania nerve the author discusses the symptoma tology of seasickness. One must distinguish between hyposensitive individuals who de velop the syndrome only during sever storms, normally sensitive ones, and hyper sensitive individuals who develop the syn drome as soon as they embark. The syn drome may appear brusquely or slowly with characteristic subjective prodromes The first subjective symptoms are a dis turbance of the mood and a desire to b left alone, followed by sensorial dulling heaviness of the limbs, facial pallor an headache. Somnolence is more frequen than insomnia, and there is muscular lassi tude. On closing the eyes the picture o oscillation continues to be seen, vertig supervenes, and the floor seems to cav in. Severe melancholia with apathy an indifference supervene, and particularly odors which are normally indifferent be come repulsive, and food is rejected com pletely. Vegetative symptoms include anx iety, sialorrhea, pallor, cold sweat, nausea vomiting, bradycardia, marked hypotonia pollakiuria followed by oliguria, and firs increased and later decreased perspiration leaving the skin dry and cold. Women may show menstrual disturbances, alway of a transitory nature. Vertigo, anxiety and nausea may be attributed to excita tion of cortical centers, pallor, deep per spiration and vomiting to excitation of th spinal cord, peristalsis, vomiting, diarrhea and bradycardia to excitation of the vagus and sialorrhea to excitation of the glosso pharyngeal and facial nerves (chorda tym pani). All this shows an organic process

most important factor of which is lo-ed in the labyrinth, with increased endo-phatic pressure, consecutive to in-ased choroid pressure and increased od pressure which is present at the et due to suprarenal discharge and pathetic vasospasm. Later bulbar cen-s are stimulated and the parasympathet-syndrome predominates.

In the hypersensitive the effects of sea-kness persist for some time after termi-ion of sea travel; some individuals show very intense syndrome but have a great pacity for recovery, and others develop y a mild syndrome from the beginning. uring the acute stage strangulation of nias and abortions have been observed, ated to the straining on vomiting, and an increased tendency to intense muscle tractions. Recovery from seasickness is mplete and there are no residual symp-ns.

Various substances have been used em-ically in the treatment of seasickness, d the most effective ones are those which oduce vasoconstriction by a sympa-romimetic effect, counteracting the vagal fects. Sedatives and hypnotics, bromides, lerian, alcohol, chloretone and opium ve been recommended, and in more ad-nced stages atropine and scopolamine. arting one week before embarkation 4 6 Gm. of alkaline bromides daily pro-hylactically have been recommended; also commended was iced champagne, and o to three capsules containing 1.0 Gm. antipyrine, 1.0 Gm. of sodium bicarbon-e and 0.6 Gm. of tartaric acid each ily. One writer recommended a simple et and abundant bowel evacuations for veral days before embarkation, and 2.0 m. of chloral hydrate or ammonium romide before embarkation; chloretone capsules of 0.3 Gm. every three to four ours, or 10 to 15 drops of validol are lso recommended. A simple mechanical eatment was advised with the idea of bolishing the movements of the otoliths; amely, a pillar suspended on a system of prings which keeps the head in a hori-ontal position by compensation of the scillations. Papaverine was introduced, nd later a 20 per cent alcoholic solution f benzyl benzoate, chloretone in a dose f 0.3 Gm., 0.5 mg. of scopolamine hydro-romide perorally or parenterally, and 1 mg. of cocaine in 30 Gm. of chloroform water. Morphine, strychnine, and atropine have also been recommended. Commercially available preparations include bellergal, bellafoline, belladenal, gynergen, and vasano which is the camphorate of scopolamine and hyoscyamine. During World War II the American army used ethyl-beta-methyl-allyl-barbituric acid in a dose of 0.1 Gm. morning and evening and thus achieved protection of 40 to 75 per cent of hypersensitive soldiers against seasickness and avoidance of dulling and impairment of combat qualities; this substance was considered a military secret and was denominated V-12. It was also used by the Canadians, in a mixture containing 130 mg. of it together with 0.1 mg. of hyoscine and 0.3 mg. of hyoscyamine hydrobromide. In the usual doses the substance may be considered nontoxic, and only in experimental animals neuritis was observed. A mixture of 0.1 mg. of hyoscine hydrobromide, 0.3 mg. of atropine sulfate and 130 mg. of sodium amytal has also been recommended.

Chloromycetin in the Treatment of Typhoid Fever. Fourteen Cases Treated in the Middle East — Cook, A. T. and Marmion, D. E.—*Lancet*, 2: 975 (November 26) 1949.

"Typhoid and paratyphoid fevers are endemic in Egypt, and tend to occur sporadically and in small outbreaks of 3 or 4 cases among military and Royal Air Force personnel and families. The 25 cases recorded here were seen between February and September, 1949. All the patients had been protected by T.A.B. inoculation, though 3 had not had booster doses within the preceding 12 months.

"The original intention was to carry out a controlled trial. However, the untreated control of the first case treated with the drug became so desperately ill that it was deemed unjustifiable to withhold chloromycetin, and there is little doubt that it saved his life. After this it was decided to give the drug only to the most severe cases.

"Future severity is difficult to assess in the early stages of typhoid, but experience showed that (1) a high maintained fever, (2) severe toxaemia with delirium, pros-

tration, and repeated vomiting, and (3) the occurrence of complications, augured unusual severity when present in the early stages of the illness; in any event such cases run a long course, imposing a heavy strain on their resources, resulting in great debility and prolonged convalescence. This was the basis of selection for chloromycetin therapy."

Salmonella typhi was isolated from the blood in all cases except 1 in which it was grown from the faeces, and 1 in which the diagnosis was confirmed by agglutination reactions.

"Of the 25 cases, 14 were treated with chloromycetin, and of these 3 had relapses which were similarly treated." In addition the writers treated 1 case each of paratyphoid A and B fevers, with results identical with those obtained in typhoid. "In 11 cases chloromycetin was not given." The 2 most severe of these occurred before the writers had the drug; 1 died of a perforation after a very stormy course, while the other relapsed 10 weeks after becoming afebrile, but eventually recovered.

"Chloromycetin was dispensed in capsules containing 0.25 Gm. for oral administration. Each course started with a dose of approximately 50 mg. per Kg. body weight (10-14 capsules). Vomiting, delirium, and lack of cooperation often made it difficult to administer this large dose, and it would have been an advantage to have a preparation for parenteral injection. In 1 case it was necessary to pass a Ryle tube and inject an aqueous suspension of the drug into the stomach. After the initial dose one capsule was given every two hours until the temperature fell to normal, and thereafter every four hours to complete the course of 20-22 Gm., varying according to the size of the patient and the response to treatment. An average course took nine days.

"General treatment followed accepted lines. Patients were nursed in air-conditioned wards at a temperature of 70-80° F. (the day temperature outside often being well over 100° F.), and small frequent feeds were given of a high calorie, low residue bland diet with adequate minerals, vitamins, and fluids. When there was respiratory infection of more than trivial degree, penicillin was given; but it was not observed to make any difference while t typhoid infection remained active.

"All treated cases were kept in bed f 14 days or more after the fever had su sided, and by this time all but the mo severe had become very active in bed (marked contrast to untreated cases). E ercises and massage were started in a cases within a week of defervescence."

The temperature is the most reliab objective guide to the progress of typho fever. The drug brought about rapid d fervescence. There is no material differenc in the speed of reaction at any stage the illness; in no case did the fever pe sist for more than five days after admi istration of the drug was started.

"In the less toxic cases the general im provement keeps pace with defervescenc but in the more severely ill it is naturall retarded." In 1 case, for example, chloro mycetin therapy began on the twenty seventh day of illness, and though de fervescence took place in 3 days, menta confusion persisted for 13 and urinary in continence for 23. "Blood pressure tende to drop as the temperature fell, but ros after a few days to a level higher than tha maintained during the febrile stage.

"Where toxaemia was relatively mild the first improvement was a subjective one headache and malaise diminished, and symptoms of respiratory infection subsid ed. This happened remarkably constantly within 48 hours. The more toxic patients who were mostly delirious responded less dramatically, but even in them some de gree of improvement was discernible on the second day of treatment: vomiting and meteorism became less troublesome, and there was generally a partial clearing of consciousness. Appetite usually began to return in 4-6 days, and was soon voracious.

"Whereas in the earlier and less severe cases the most striking effect of chloro mycetin is the curtailing of the length of illness, in the later and very severe cases the accent is on the saving of life." Two cases were regarded as moribund at or soon after the beginning of chloromycetin therapy, and 1 case was almost as desperately ill during her relapse. In the writers' opinion these patients would have been unlikely to recover without chloromycetin.

n the 3 relapses in the treated cases
oromycetin was just as effective as in
original attack. It is noteworthy that
severe respiratory infection that was
most important feature of 1 relapse
ponded within five days of the start of
oromycetin therapy, pari passu with
signs and symptoms of abdominal in-
tion and toxaemia. "Though penicillin
s given in this case there was a strong
nical impression that the relief of ty-
hid toxaemia by chloromycetin was the
dominant factor permitting recovery of
concomitant respiratory infection.

"The effect of chloromycetin on com-
cations cannot be judged on so small
eries. The complications of extreme de-
ty (bedsores, skin sepsis, parotitis, etc.)
uld, of course, be reduced almost to
nishing point. . . . Respiratory infection
hich is so constantly present that it
uld be looked on as part of the disease
her than as a complication) was usually
ieved by chloromycetin, like the other
nical manifestations of typhoid fever."
rforation did not occur in any treated
es, but there was intestinal haemorrhage
ring treatment in 1 patient and after
atment in another, coinciding with the
et of a relapse.

'Clinically speaking, the effect of chloro-
cetin seems to be to arrest the disease
whatever stage it has reached, and to
rilise the blood at the same time;
fervescence takes place within five days,
d convalescence then starts. In conse-
ence a patient treated fairly early in
illness is spared much of the drawn-
t fever and toxaemia associated with
classical picture of typhoid, and begins
convalescence with relatively little de-
ity. He also has much more strength
h which to meet late complications and
apse, if they occur. After 14 days free
fever it is usually necessary to curtail
her than encourage activity, and the
ly return of appetite is noteworthy. It
fair, in fact, to say that the period of
nvalescence is halved by treatment with
loromycetin within the first two weeks
the illness."

As regards late cases, so much damage
s already been done here that the accent
inevitably on the saving of life; but
en in these cases the total length of the
ness must be considerably diminished.

"No toxic effects were observed in patients given chloromycetin. Nausea and vomiting were present, if at all, before the drug was given. No particular effects were noted on the blood picture or the urine.

"It is obvious but worthy of comment that chloromycetin considerably eases the heavy burden that typhoid fever imposes upon the nursing staff, and in these days of universal shortage of nurses this is not the least of the benefits it confers."

Local Action of Oxygen in Burns — Montoya Miranda, Arturo — *America clinica*, 15: 500 (December) 1949.

After severe burns irrigation of the tissues is reduced or lacking and the cells of the involved areas are unable to get rid of carbon dioxide and to take up oxygen, leading to diffusion of the former and to asphyxia and death of the cells, in addition to the direct destruction of the burned cells. In the anaerobic life of the cells certain chemical phenomena take place without intervention of oxygen, the latter acting secondarily. Due to anaerobic life organic substances are decomposed and give rise to products of reduction and this facilitates subsequent combustions; the products of reduction are in better condition to take up the oxygen from the so-called auto-oxidizers which take up the oxygen from the blood. Many of the products of decomposition and reduction are toxic and their accumulation leads to severe intoxications. In burns, oxygen becomes scarce and the auto-oxidizers cannot act on the toxic products of anaerobic life, increasing the toxemia. Oxygen treatment is based on these considerations.

Burns are traumatic lesions similar to other wounds, but with some peculiarities among them the large loss of fluid through the burned surface, and the large amount of dead tissue which increases asphyxia and lack of oxygen. Proteolysis of the dead tissues adds more toxic substances. Local treatment will favorably modify shock, toxemia, infection and other complications. Complete removal of all burned tissues followed by suture is not feasible and dead tissue, slowly eliminated, remains; attempts to detach it lead to hemorrhages and increased traumatization be-

cause of its firm attachments. The dead tissue is a good medium for germs. The toxemia is attributable to the products derived from the anaerobic life, and accumulation of carbon dioxide is also responsible for systemic disturbances and complications. Many toxic substances affect the vegetative nervous system, producing shock. The author distinguishes only superficial and deep burns, the latter involving destruction of the skin, and sometimes the deeper layers. Superficial burns are more painful than the deep ones as the nerve endings are not destroyed, but exposed. Burns have a tendency to slow healing and to chronic ulcerations, retraction, adhesions and symphysis depending on extent and infection. Retraction is caused by abundant insoluble toxic substances formed during proteolysis and cicatrization. All these points justify the importance of local oxygen treatment of burns. The author has used this treatment in all traumatic lesions, particularly those with lacking or delayed healing, with highly satisfactory results. The author observed that when oxygen is brought to the burned area under a certain pressure and constantly the lesion will remain dry and a kind of brilliant varnish will form, similar to that of wounds at the end of cicatrization, and cicatrization may supervene rapidly, without loss of fluid. Rapid results were obtained in all superficial burns with pressure oxygen application every two to three hours. In deep burns the oxygen was applied under pressure every hour to two hours, resulting in a favorable course, and rapid elimination of the dead tissues which could be detached readily. The oxygen is used directly from the cylinder and distance, direction of the jet and pressure must be regulated in such a manner that no pain is produced. The main goal of local treatment of burns has been to produce coagulation in order to avoid loss of fluid, infection and other complications but in the author's opinion this method does not comply with one of the requisites of the treatment of any traumatic lesion; namely, strict cleanliness. Many of the local applications used, macerate the tissues, cause irritation and impede penetration of other substances. Liquefied organic materials and other secretions accumulate underneath the coagulated layer and their decomposition produces a bad odor; they also constitute excellent culture medium for germs. I is often encountered when the coagula layer is removed. The secretions irrit adjacent areas and cause pruritus. Inte absorption of toxins impairs the gene condition. The author has seen numer cases in which immediate surgical toile furnished better results. Continuous pr sure oxygen application achieves forn tion of a protective layer without any these inconveniences, and this layer v assume the aspect of newly formed pseu epithelium; its flexible character will av retractions and deformations and gra can be applied.

The author interprets the oxygen eff as one of colloidal nature, with conden tion of the proplasmatic colloid; und neath the protective layer cicatrization the burn is rapid and without compli tions. Loss of fluid is prevented by the pr tective layer, particularly in superfic burns, and the tissues preserve their ela ticity which is not the case with coagula treatment. In deep burns oxygen treatme must be carried out with greater intensi in order to keep them dry. Sometimes clean smooth uniform brilliant dry y low scab will gradually form and on i detachment cicatrization will be complet The dead tissues can be removed witho danger. Continuous use of oxygen has disinfectant action. Toxic substances a destroyed diminishing the toxemia. T lesion turns red on oxygen application i dicating the circulatory benefits and t avoidance of tissue asphyxia. Putrefactio of dead organic material and anaerob infections are avoided by the destructio of the toxic substances. The oxygen al stimulates the young cells. The lesion kept clean, germs will not multiply muc and bad odor will be suppressed. Earl grafts are afforded. Dressings are simp and painless. The scars are soft and elasti due to prompt elimination of injured ti sue.

In the author's hospital service burn are immediately gently lavaged with steril water and disinfectant ichthyol soap, in cluding the area around the burn, an then the latter is lavaged with alcohol an ether without touching the burn; in super ficial and extremely painful burns isotoni saline solution containing 1 per cent o

vocain is used. The burns are then ed carefully. If scabs have formed lav- is repeated frequently in order to oid infection. The oxygen is then applied, ery two to three hours in superficial rns and every hour to two hours in ep burns, with increased pressure and ration in the latter case. Disinfectants d colored antiseptics are absolutely oided. Exceptionally sulfadiazine is used ally if there is not much dead tissue d the blood supply is fairly good. The fonamides frequently do not dissolve t cake and then act as foreign bodies. a disinfectant is necessary Dakin's solu- n is preferred, particularly when there a large amount of dead tissue and in- ction is imminent or already present. e burns are lavaged daily with saline lution, removing any element which may pede the direct effect of the oxygen on e burned surface. Dead tissues are care- lly removed but if hemorrhage is feared tachment by the action of the oxygen waited for. Grafts are done early. No uze is applied to the burns but they are otected by an arc covered with cloth. xygen application is continued after scar rmation with increased pressure as this sults in mobilization of the tissues.

Among a total of 30 superficial burns nd 22 deep burns there was only 1 death.

ariation in the Duration of Tuberculin Skin Sensitivity Produced by Two Strains of BCG — JACOX, RALPH F. AND MEADE, GORDON M. — *American Review of Tuberculosis*, 60: 541 (November) 1949.

"In this study, two groups of individuals ere vaccinated with BCG (Bacillus Calmette-Guérin) vaccine obtained from two ifferent sources. Group A consisted of 03 nurses and medical students with an ge distribution of 18 to 26 years. These ndividuals were vaccinated in September 946 with a strain of BCG (Vaccine A). . . It contained 15 mg. of bacteria in ach ml., was shipped in refrigerated conainer, and arrived two days after preparaion (12 hours after leaving the laboratory f origin). Upon arrival it was immediatey placed under refrigeration. Vaccination as then carried out 24 to 48 hours later by the percutaneous method described by Rosenthal.

"All individuals were examined two weeks after vaccination and, with few exceptions, were noted to have developed a characteristic papular eruption at the site of inoculation. Tuberculin tests were performed at 1, 3, 6, 9, and 12 month intervals from the time of vaccination."

"One month after vaccination, a well developed skin sensitivity (2 or 3 plus) to 0.005 mg. of PPD was observed in 88.3 per cent of the vaccinated individuals.

"Three months after vaccination, 79.2 per cent reacted to 0.005 mg. of PPD. In addition, a decreased intensity of skin reaction was observed. Most of the vaccinated individuals had declined from a 2 or 3 plus reaction to 1 plus or a questionable reaction. In order to exclude decreased potency in the testing material as a cause for the decreased tuberculin reactions, 0.005 mg. of PPD and 1.0 mg. of O.T. were compared by injecting each substance into different sites on the same forearm. A more intense tuberculin reaction resulted when 1.0 mg. of O.T. was used. In all subsequent tuberculin tests, only O.T. (0.1 mg. followed by 1.0 mg. if 0.1 mg. gave a negative reaction) was employed for determining tuberculin sensitivity.

"Six months after vaccination, 38.8 per cent of the vaccinated individuals had a positive reaction to 1.0 mg. of O.T. The potency of tuberculin was again tested by comparing three different commercial tuberculins for ability to produce a positive skin reaction. No variation was detected, which seems to exclude the tuberculin as a factor responsible for the marked reduction in positive reactors.

"The progressive decline in tuberculin skin sensitivity continued and nine months after vaccination only 11.6 per cent of group A were positive reactors. Twelve months after vaccination, only 10.7 per cent had a positive tuberculin reaction to 1.0 mg. O.T. If those who had doubtful reactions are included, only 18.6 per cent demonstrated a positive tuberculin reaction one year after administration of vaccine A.

"Group B consisted of 178 medical students and nurses with the same age distribution as group A. Of these, 100 had never received BCG vaccination. Seventy-

eight of this group had been vaccinated in September 1946 with Vaccine A. They had previously developed a positive tuberculin reaction as a result of vaccination but had reverted to a negative reaction by the end of a year or less. All individuals in group B were vaccinated in September 1947 with a vaccine prepared in another recognized laboratory. Vaccine B was made under carefully controlled conditions and under the supervision of an individual who has had long experience in BCG preparation and use." This vaccine, containing 20 mg. of bacteria per cc., reached the writers (unrefrigerated) 24 to 36 hours after shipment. "It was immediately placed under refrigeration and used 24 to 96 hours later. Vaccine B was administered in exactly the same manner as Vaccine A. Similarly, all individuals were observed two weeks after vaccination and were found to have developed a characteristic papular reaction at the vaccination site.

"It was observed, however, that Vaccine B produced a more intense and prolonged local reaction than Vaccine A. Several individuals developed small, suppurating lesions at the vaccination site which persisted for several months. The increased local reaction occurred with the same frequency in the individuals vaccinated for the first time as in those revaccinated one year after a previous vaccination with Vaccine A. It is of note, moreover, that nor of those who were revaccinated showe any accelerated or Koch-like reaction t suggest that any residuum of sensitivit remained.

"The duration of sensitivity in group I was determined in the same manner a described for group A (0.1 mg. of O.T followed by 1.0 mg. if 0.1 mg. gave a neg ative reaction)." One hundred per cent o group B were found to have developed sensitivity to tuberculin three months after vaccination. "One year after vaccination, 91.5 per cent of those vaccinated still reacted to tuberculin with a clearcut, positive skin test, 2.8 per cent had definitely negative reactions, and 5.7 per cent had doubtful reactions. Of the 91.5 per cent who were positive to tuberculin, 73.5 per cent reacted to 0.1 mg. of O.T., while the remainder required 1.0 mg. to elicit a positive reaction. It is apparent that the number of individuals in group B who maintained a positive tuberculin sensitivity one year after vaccination is in decided contrast to the results obtained in group A."

"The results of this study appear to support the conclusion that a strain difference of BCG will influence the vaccine's effectiveness as a sensitizing agent. If sensitivity is a reflection of immunity, it is felt that a suitable method of control of the sensitizing potency of BCG vaccine should be set up."

Pediatrics

te Respiratory Infections in Infants — Bonham-Carter, R. E. — *Practitioner*, 163: 502 (December) 1949.

The division of respiratory infections upper and lower, meaning the pharynx larynx upon the one hand, and the hea, bronchi, bronchioles, lung parenna and pleura on the other, although trary, serves a useful clinical purpose. arbitrary because in most of these inions both upper and lower respiratory ts are involved.

Upper Respiratory Infections.—The yzas: In infants, the common cold to be taken more seriously than in life, for although it is not a frequent se of illness in newborn babies, yet lemics of diarrhoea and vomiting in series have been traced to colds among hers or staff. And in this group, too, are more often followed by pneumonia at any other time, except old age.

The fact that in neonates and infants za does not always present with sneezrunning nose and cough, but instead n misleads the clinician by presenting a refusal of food, loss of weight, exia, or alarming diarrhoea and vomit- makes recognition of the symptoms ortant. The diagnosis can only be made inspection of the nose and throat, where ery red mucous membrane, sometimes h pus follicles upon the tonsils and ocionally with a postnasal drip of muco-, will be seen. During this inspection it st be remembered that a yelling baby a very red pharyngeal mucosa. Postal and throat swabs usually grow mixed anisms, but in neonates, *Staphylococcus eus* will often be found.

In the newborn, weakly babies, or preture infants, these infections must be en seriously and treated promptly, and s worth while giving penicillin and sulnamides in full doses to prevent comcations. In older babies, little can be e except symptomatic treatment; keepthe child indoors and, if necessary bese of pyrexia, in bed. In both groups, regation from other children of the e age is desirable. In obstetric hospitals these babies should be isolated, preferably with their mothers. Day nursery children should not be allowed to attend and so infect the whole nursery.

"Diarrhoea and vomiting is the most dangerous complication of these common infections. When it happens, correction of the fluid loss by mouth, subcutaneously or intravenously, must be undertaken at once and the loss of salts also promptly corrected. A solution of half-strength normal saline with 5 per cent glucose added is simple to obtain, and may be given by mouth in these cases. Breast-fed babies should not be taken off the breast, but if there is difficulty in sucking, the nose may be kept clear with a solution of ephedrine, 1/2 per cent, and sulphacetamide, 10 per cent, in saline, two or three drops in each nostril before each feed, and when the nose is blocked.

"The ease with which young infants get otitis media makes it necessary to examine the ear drums regularly, at least daily. Although otitis media may be insidious in onset, it should always be suspected in any child with recurrent bouts of screaming or crying, whether or not there is an upper respiratory infection. In infants, it is better to do a diagnostic myringotomy when a doubtful drum is seen, than to wait for the drum to bulge. After the myringotomy has been done, care must be taken that the wound is not closed again in a few hours by sticky secretions. This is particularly likely to happen in dehydrated infants. The myringotomy may be kept open by gentle syringing with saline from a soft rubber rat-tailed syringe, and may be necessary as often as two hourly.

"Tonsillitis: Infection of the lymphatic tissue of the nasopharynx is a common cause of illness in infancy, although more common over the age of 6 months. . . . The inflamed mucous membrane and pus follicles, or even a purulent membrane, may be seen on inspecting the throat. The treatment is the same as for the coryzas and their complications, but more attention can be paid to the results of throat swabs, which should be taken to exclude diphtheria in all cases when a membrane is seen. Here again, a careful

watch must be kept upon the ears, for otitis media is even more likely when tonsillitis is present.

"Lower Respiratory Infections.—Bronchitis: The presence of palpable or audible rhonchi all over the chest, when these are sonorous and give the impression of mucus flapping about in large bronchi, justifies the diagnosis of bronchitis, but care must be taken in case these loud noises overlie and make inaudible the fine rhonchi of bronchiolitis, the crepitations of pneumonia, or the signs of collapse, for it is only when these are present that a serious view need be taken.

"Little can be done for the treatment of bronchitis in infants, except prevention of the spread of infection to the smaller bronchi and lung tissue. The difficulty of giving liquefying expectorants makes the dictum that they are useless save in emetic doses true in this age group. Certainly a vomit results in coughing, which clears the chest. Postural drainage in infants is difficult to maintain, and it is dangerous to nurse a sick infant on his face tipped over a pillow, for he may suffocate. Nurse the child on his back with the end of the cot raised a foot or so and with his feet tied by a loose flannel bandage to the cot to prevent sliding up the bed. This position will not drain the upper lobe or posterior bronchi, but if the child's position is frequently changed and he is set up for feeding and so on, it is adequate. Steam is probably the best method of liquefying bronchial secretions, and a kettle placed at a safe distance, at least 3 feet from the baby, allowing its steam to circulate under a tent of blankets, is the method of choice. Compound tincture of benzoin, 60 minims (3.5 ml.) to 1 pint of water, may be added to the kettle.

"Bronchiolitis: The extension of the inflammatory process into the smaller bronchioles is serious. It is the forerunner of lobular collapse of lung and subsequent infection and bronchopneumonia. Its treatment does not differ except that sulphonamides and penicillin should be given at once. Cyanosis may be treated with oxygen in a tent or box or, if these are not available, by bilateral nasal catheter. It is often difficult to determine whether oxygen for cyanosis or steam to liquefy secretions is the proper treatment. The rule here is that if oxygen relieves cyanosis it is correct; if it does not it should be assumed that it is not reaching the alveoli, and bronchoscopic aspiration must be tried. Little is to be gained by the use of atropine or other drugs used in the attempt to reduce bronchial secretion, for these render the secretion more viscid and more likely to block the bronchi."

Acute Laryngotracheobronchitis: This dangerous disease attacks principally children under the age of 2 years and only 5 per cent of cases occur over the age of 6. "Boys are affected nearly twice as often as girls. The untreated mortality rate is 80 per cent. The onset is sudden and the course rapid. An infant with a croupy cough, with or without coryza, develops increasing respiratory obstruction with stridor, at first inspiratory, and later both inspiratory and expiratory. There are bronchitic signs all over the chest and sometimes patches of collapse. Cyanosis, sometimes of the 'heliotrope' colour described in the 1918 epidemic of influenza, develops quickly and asphyxial death occurs in 24 to 72 hours if nothing is done. Several authors recommend early tracheotomy for spasmodic croup, with frequent bronchoscopic drainage. "Penicillin and sulphonamides should be used, but as these authors base their belief in the viral etiology of the disease partly upon the inefficacy of these drugs, they can only be used with the object of preventing secondary infection. After bronchoscopic drainage, oxygen can be used to relieve cyanosis. Postmortem material shows an inflammation of the whole respiratory tract from the pharynx to the smallest bronchiole, involving the cords and sometimes so intense as to cause massive sloughing." Several authors have suggested using chloromycetin, 0.25 Gm. four hourly, for this condition.

Pneumonia.—(1) Acute Specific Pneumonias: Staphylococcal Pneumonia. "In the newborn, pneumonia, which may be either lobular or lobar in distribution, is the result of neonatal sepsis giving rise to a staphylococcal septicaemia. The occurrence of this condition in infants' wards or nurseries must be regarded as a failure in the technique of nursing the newborn.

Treatment must be prompt, and should started as soon as any signs are ob- ed in the chest. No delay pending exact nosis or radiological examination can llowed. The dosage of penicillin and honamides should be at the highest l, and every device to isolate the nism and find its sensitivity to sul- namides and the antibiotics must be l, for so many of these staphylococci resistant. If the organism is isolated nursery or ward it must be tracked n to its origin and eliminated. The y should be isolated, preferably with mother, and nursed with the precau- s usual in infectious illness. Postnasal bs and repeated blood cultures may ecessary to obtain the infecting organ- When an organism resistant to sul- namide and penicillin is found, strep- ycin in doses of 0.02 Gm. per pound 044 Gm. per Kg.) body weight per , divided into aliquot doses and given amuscularly at six hourly intervals, y be used for a maximum period of c days, by which time the organism have been knocked out, or have be- ie resistant to streptomycin also. Aureo- in and the new antibiotics have yet be tried in these infections, but they l out good hope of success and are h less toxic than streptomycin.

Empyema and lung abscess are com- n complications. Air-containing, cyst- cavities also develop, which can be n to regress slowly with treatment."

Pneumococcal Pneumonia. Penicillin and honamides should both be given in full es to children with lobar pneumonia. n oxygen tent (or box) for cyanosis, l brandy in doses of 5 to 10 minims 3 to 0.6 ml.) for circulatory failure, stitute the treatment. Penicillin and honamides should be given until the perature, respiration rate and pulse e been normal for three days; usually y fall dramatically within the first 48 rs."

The complication of empyema in infants to pneumococci and streptococci has ome much less frequent since the in- duction of penicillin and sulphonamides, hardly any reduction has occurred in incidence of staphylococcal empyema.

"The frequency with which otitis media nplicates pneumonia in infants makes regular inspection of the drums a necessity. It is a frequent cause of sustained temperature after 48 hours of treatment."

"(2) Aspiration Pneumonias: Inhalation Pneumonia. Lipoid pneumonia is a common postmortem finding in milk-fed infants, but it seldom presents itself clinically. The inhalation of milk which may give rise to it is not uncommon in weakly infants, and the immediate treatment of this is bronchoscopic drainage, with postural drainage and full doses of penicillin and sulphonamides. The extension of a bronchitic process to involve the lung alveoli is probably preceded by blockage of bronchioles and collapse of small areas of lung, with subsequent infection, giving rise to diffuse lobular or bronchopneumonia. This condition may be caused by any organism, but again the staphylococcus is the most common in the newborn.

"The story in infancy is that of a baby who gets a cold which affects his chest, and who, instead of throwing it off in a week or so, becomes progressively more ill and develops areas of dulness with patches of crepitation and bronchial breathing throughout the chest. The differential diagnosis from an acute asthmatic attack may be difficult, but the presence of many musical rhonchi should lead one to suspect asthma. The treatment is the same as for pneumococcal pneumonia, but the prognosis is not so good.

"Other Lower Respiratory Diseases.—Collapse of Lung: This is a frequent complication of any upper or lower respiratory infection in this age group. It is diagnosed radiographically after finding physical signs resembling either those of fluid or consolidation. A shift of the mediastinum towards the side of the collapse which can be made out clinically is rare in infants.

"If the child is not febrile, and there is no reason to suppose that the collapsed area is infected, treatment should be directed solely towards getting the lung to reexpand. Frequent changes of posture, tipping the baby over the knee, and firmly clapping the chest wall several times daily usually result in reexpansion; but if this fails, bronchoscopic aspiration of the obstructing mucous plug should be done early, before the collapsed lung becomes grossly infected. After the lung has be-

come infected, the same efforts to get it to reexpand must be made, coupled with treatment as for pneumonia.

"Obstructive Emphysema: Sometimes when a mucous plug partially, but not completely, blocks a bronchus, air can be inspired past the obstruction but cannot be expired again because of the weakness of the expiratory effort. This can occur with or without obstructive collapse, but when massive, will cause collapse of lung by pressure, with mediastinal shifting, and cardiac embarrassment. The physical signs are a blowing out of one side of the chest, with a tympanitic note over it and a diminished air entry, but these signs are only present in the most extensive cases. The minor degrees will respond to the expectant treatment of collapse, but in the extensive case, removal of the plug by bronchoscopy may be necessary.

"Pneumothorax: This is not an uncommon finding in newborn babies with a little respiratory embarrassment. In such cases it quickly absorbs spontaneously and the only treatment necessary is oxygen for the respiratory embarrassment. When, however, it complicates neonatal pneumonia, it may be caused by the rupture of a small staphylococcal abscess and be accompanied by an empyema; then the treatment is the same as for empyema."

Empyema: It has been shown that in infants, staphylococcal empyemas are at least as frequent if not slightly more frequent, than pneumococcal. "These infections occur in the neonatal period and are then a manifestation of neonatal sepsis. In older children they are a complication of pneumonia.

"Repeated aspiration of the pleural cavity, using local anaesthesia and a wide-bore needle, and replacing the fluid wi drawn by a solution of penicillin of slig ly less volume containing up to 50,0 units, combined with systemic sulpho mide and penicillin in full doses, is initial treatment. In some cases, about ha no other treatment is needed, but wh the pus becomes thick and cannot be pirated, an intercostal catheter may ha to be introduced, and later more extensi surgical drainage with breaking down loculations may have to be done. Aspir tion treatment is controlled by repeat x-rays to assess the amount of pus remai ing after each aspiration. Again, the orga ism must be looked for at the first aspir tion and its sensitivity to sulphonamid and penicillin ascertained. The other an biotics may be used if a resistant organis is found."

Whooping Cough: "The disease mu be suspected in any infant with a spa modic cough and vomiting, with or wit out a contact history. A cough plate w clinch the diagnosis in the early stages, a a lymphocytosis up to 30,000 is corrobora ing evidence. Sometimes the organism c be recovered by causing a cough by tic ling the back of the pharynx with a cam hair brush and plating the result. The mo tality of this disease is largely from t complication of aspiration pneumonia, that a good case can be made out f prophylactic use of penicillin and sulphon mides in the early stages of the disea in infants.

"In any child who has a recurre whooping cough-like cough, especiall when this is associated with diarrhoe cystic fibrosis of the pancreas should b suspected."

Treatment

Sulphonamides	Penicillin
2 grains (0.13 g.) per pound (0.3 g. per Kg.) body weight daily, divided into aliquot doses at four to six hourly intervals throughout the 24 hours, with twice this amount as the initial dose.	By mouth, 20,000 units per pound (44,00 units per Kg.) body weight per day, give upon an empty stomach at four hourly in tervals. By intramuscular injections, 4,00 units per pound (8,800 units per Kg.) c body weight per day, divided into aliquo doses at four to six hourly intervals through out the 24 hours.

The oral route is only contraindicated
abies under 6 months when there is
iting. The antibiotic is best given in
ly prepared solution of high concen-
on by teaspoon.

Other Antibiotics: These may be used
ases in which the organism is found to
enicillin and sulphonamide-resistant.

Streptomycin, 0.02 Gm. per pound
44 Gm. per Kg.) body weight daily,
ded into aliquot doses given intra-
cularly six hourly.

Chloromycetin, 0.05 Gm. per pound
1 Gm. per Kg.) body weight, every
e hours by mouth.

Aureomycin, 0.005 Gm. per pound
11 Gm. per Kg.) body weight, every
hours by mouth.

Chloromycetin and aureomycin are dis-
ed in capsules, the contents of which
be turned out and suspended in water
ucilage for administration by mouth.

Fluids: Any infant with a respiratory
ction is likely to be dehydrated by con-
itant diarrhoea and vomiting, and this
t always be corrected by extra fluid
mouth, if this is possible, or subcuta-
sly or intravenously. This is particu-
y important when large doses of sul-
namides are being given, if crystalluria
its complications are to be avoided.
n the whole, the more soluble com-
nds, sulphamezathine or sulphatriad,
preferable in such cases."

rophylaxis.—It has been found in day
series, that daily doses of 0.25 to 0.5
of sulphonamides, according to age,
cut down the incidence of respiratory
ctions, presumably by cutting down
secondary infection, for it cannot help
virus coryzas. "Similar studies using
ffered tablet of 50,000 units of penicil-
by mouth have been done. It seems
btful, however, because of the preva-
e of *Staph. aureus* in this age group,
because this organism is so often
nd to be resistant to penicillin and sul-
namides, if this treatment should be
l in a closed community."

everal authors have shown in a series
studies in day nurseries that a rise of
moglobin of the order of 6 per cent
accompanied by a reduction of 20
cent in the absentee rate. "They con-
le that the anaemia affecting these
dren was nutritional and correctable by iron therapy, and that the prophylaxis of anaemia in day nursery infants was capable of producing a striking reduction in the morbidity rate.

"In infants with second class respiratory mucosa, who are particularly likely to have respiratory infections, it is wise to double the ordinary dose of cod liver oil because of the possibility that vitamin A may, in increased doses, help them to avoid repeated infection.

"Lastly, there is a group of children within this age group who are particularly liable to respiratory infection. These are premature infants in the first two years of life, other small birth weight babies, infants with rickets, coeliac disease, and cystic fibrosis of the pancreas, but in addition to these, there are infants with second rate respiratory mucosa who suffer from none of these diseases, but get every infection that is going. All these children should be given iron and increased vitamins A and D."

Hemorrhagic Manifestations in the Newborn — Peña Ramos, Eleodoro — *Archivos del Hospital clínico de niños Roberto del Río,* 17: 66 (June) 1949.

The frequency of hemorrhagic manifestations in the newborn has been known for 200 years but its study has gained new interest with the discovery of vitamin K and the establishment of a constant transitory hypoprothrombinemia in the newborn; basically the latter would depend on vitamin K deficiency but its origin and appearance have been interpreted in various ways, including immaturity of the liver function, and exhaustion of the reserves transferred from the mother, while bacterial pullulation in the intestinal tract after its original aseptic character, and supply in the milk would account for the subsequent restoration of normal prothrombin values. Administration of vitamin K to the mother during delivery or to the infant immediately after delivery is known to prevent the hypoprothrombinemia; it has been hoped that systematic vitamin K prophylaxis would prevent hemorrhagic disease of the newborn but studies on large numbers of cases have not confirmed this hope. Therefore it must

be assumed that the hypoprothrombinemia of the newborn is only a background on which other factors become effective in the mechanism of hemorrhagic disease, including infection, asphyxia, traumatism and poor ligature of the cord, while idiopathic hypoprothrombinemia is the cause of neither the majority nor the most important hemorrhages.

The author studied on 1,640 newborns' prothrombin time, the factor of vascular fragility, the clinic and anatomy of frank and occult hemorrhages, and the effect of vitamin K. In 250 newborns the prothrombin time was determined daily until it reached or fell below the maternal level. In 63 normal newborns with a birth weight above 2,500 Gm., without history of trauma, and vitamin K injection, and free of infections and hemorrhages a total of 376 determinations was carried out; they showed large variations and the prothrombin time was frequently 50 to 70 seconds and more, while values above 80 seconds were exceptional and 1 case showed a value of 133 seconds. Thus there is a wide margin of security.

With injection of 6.4 or 10 mg. of vitamin K into the mother within 24 hours before delivery the infants showed a virtually flat prothrombin time curve. The maximal and minimal values found that each day differed little when the mother was given 6.4 mg., and hardly at all when the mother was given 10 mg., while they showed large variations in the untreated cases. The results with administration of 3.2 mg. to the infant either perorally or parenterally hardly differed from those obtained by maternal administration. The experience with prematures was limited as the majority showed hemorrhages, infections, or a history of vitamin K injection.

The author then deals with newborns with hemorrhagic manifestations, first with the group of 6 cases in which the heel puncture for obtaining blood bled profusely. In 3 of these 6 cases association with other important conditions was dealt with, including syphilis and septic infection. The prothrombin time was increased in this group; in some cases of this group the hemorrhage stopped spontaneously although the prothrombin time increased, while in others vitamin K had to be injected, resulting in prompt control of the hemorrhage and effect on the prothrombin time.

In hemorrhagic disease of the newborn the prothrombin time was always very high, always exceeding 100 seconds, and usually 200 seconds.

In cephalhematoma the prothrombin time was slightly above normal during the first few days, with recovery around the tenth day; in 2 cases the mother had received vitamin K and the prothrombin time was low.

Retinal, subconjunctival and vaginal hemorrhages, scanty melena and scanty umbilical bleeding showed the same prothrombin times as normal newborns, depending on whether mother or infant had received vitamin K, and these hemorrhagic manifestations therefore showed no relation to the prothrombin level. There was only 1 exception; namely, a case of scanty umbilical hemorrhage in a noninjected infant in whom the prothrombin time stayed relatively high until the tenth day.

In a small group of various hemorrhages from ear and bladder, hemorrhagic vomiting, and petechiae and hematomas no marked deviation of the prothrombin time from the norm was encountered.

With respect to infections conjunctivitis showed normal prothrombin times while congenital syphilis showed a marked increase; in view of the fact that vascular fragility was not encountered in congenital syphilis the tendency to hemorrhages in this disease must be attributed to hypoprothrombinemia, and the latter may be due to the hepatic lesions. In obstetric trauma the prothrombin time depended on the administration of vitamin K. In 3 sets of biovular twins the prothrombin times were highly similar in both infants.

The vascular factor was tested with a suction apparatus provided with a glass bell of 1 cm. diameter, applied with a negative pressure of 25 cm. of mercury to the flexor surface of the elbow; this proved superior to the Rumpel-Leede test. The test was always negative indicating that vascular fragility plays no part in hemorrhagic disease of the newborn. The material included 8 cases of hemorrhagic disease of the newborn, 6 of bleeding from the puncture wound, 22 of cephalhematoma, 42 of retinal hemorrhage, 41 of subconjunctival hemorrhage, 8 of scanty

ena, 85 of occult intestinal hemorrhage, each of scanty umbilical and vaginal ding, 1 of hematuria, 19 traumatic morrhages, 8 of petechiae, 4 of sanholent vomiting, and 27 hemorrhages nd on autopsy. The etiopathogenesis ot uniform and hypoprothrombinemia be excluded in many cases. The term hemorrhagic disease of the newborn is sharply defined; thus some authors ude intracranial hemorrhages which ually are caused by obstetric trauma. e cases of bleeding from the puncture nd actually constitute potential hemorgic disease. The relatively small number cases of hemorrhagic disease of the new- n compared to that of other hemorges indicates that not too much should expected from prophylaxis by routine amin K administration. Of the 8 cases, nvolved newborns with a birth weight 3,500 Gm., while the remaining 6 had birth weight below 2,850 Gm., and 3 of m could be considered as prematures, ghing less than 2,500 Gm. The hemorgic character of certain bronchopneunias disappeared with routine admin- ation of vitamin K to prematures. Two ants showed definite infection, 1 of them hilis and the other jaundice and omphas, with a hemorrhagic syndrome and rked elevation of the normal prothrom- time at first taken on the sixteenth y; the mother had received vitamin K. us infection seems to be more important n hypoprothrombinemia. The hemorages appeared in 5 cases before the rth day, and in the others on the ninth, th, and sixteenth days respectively. All t 1 of the infants showed more than e manifestation of hemorrhage. There re no deaths.

Cephalhematoma was never associated th any other hemorrhagic manifestation d did not interfere with the general con- ion; obstetric procedures were men- ned in 5 of the 22 cases. The blood of cephalhematoma contains more erythrotes per cubic millimeter than the circulat- blood, a normal number of platelets d less fibrinogen; it does not coagulate th an excess of calcium or thromboplas-, and antithrombins do not play a part the lack of coagulability either.

Rentinal hemorrhages were found in 42 t of 300 infants examined around the fourth day, 10 on the right, 13 on the left, and 19 bilaterally. The incidence of retinal hemorrhages was 17.5 per cent among 91 infants whose mothers had received vitamin K, and 12.5 per cent among 209 whose mothers had not received it. Together with the prothrombin time findings this indicates that there is no relation between retinal hemorrhage and hemorrhagic disease of the newborn. Subconjunctival hemorrhage could also be excluded from hemorrhagic disease of the newborn. With the same criteria of incidence in relation to vitamin K treatment of the mothers and the prothrombin time scanty melena and occult intestinal hemorrhage do not belong in the hemorrhagic disease of the newborn. The cases of scanty umbilical hemorrhage occurred usually after the sixth day and therefore suggest no relationship to prothrombinemia but the prothrombin time in these cases showed a special tendency to remain around 50 to 60 seconds beyond the usual time; however this type of hemorrhage is insignificant, occurs in babies of mothers who have received vitamin K and who therefore have a normal prothrombin time as well. Vaginal hemorrhages were always discrete, rarely lasted more than two days, and occurred between the fourth and seventh days; it was associated with hemorrhagic disease of the newborn in 2 cases, preceding it in 1 and following it in the other, and with umbilical bleeding in 2 other cases. One of two hematurias was associated with hemorrhagic disease. Vaginal and vesical bleeding seem caused by hormonal factors, and become more severe and intense when associated with hemorrhagic disease. The traumatic hemorrhages appeared from the first day and did not show any subsequent intensification. Hemorrhagic vomiting was caused by cracks of the maternal nipples in 2 cases, and probably by swallowing of blood during delivery in 2 other cases; the prothrombin time showed no alterations. Some form of hemorrhage was encountered in 27 autopsies, including at least 19 prematures while in 4 no data as to prematurity were available and 4 were term babies.

These hemorrhages have little relationship to hypoprothrombinemia; thus 15 of the deaths occurred on the first day of life when hypoprothrombinemia is absent

or just starting to appear, only 6 deaths occurred on the second and third day when hypoprothrombinemia is at its peak, and the remaining 6 occurred between the eighth and twenty-seventh days when the prothrombin has recovered. Of the 15 deaths of the first day in 10 severe hemorrhages of the nervous system were encountered and a suprarenal hemorrhage in 1, while 4 showed petechial manifestations evidently dependent on asphyxia. Thus these deaths must be attributed to obstetric trauma particularly as mostly premature were involved. Only 9 of the 27 cases showed a history of a more or less difficult delivery, including four podalic presentations, three cesarean sections, one internal version and one forceps, but it is known that for the immature constitution of prematures the physiological birth trauma may denote a severe danger. Of the 27 babies 9 had had vitamin K prophylaxis, and in 4 of them the hemorrhage involved the central nervous system, sometimes with extensive tears so that no treatment could possibly have prevented the hemorrhage. Finally in a good number of cases the hemorrhages encountered on autopsy were insignificant and played no part in the causation of death; the latter was caused by bronchopneumonia or by prematurity in itself.

Vitamin K prophylaxis of the mother or the baby itself avoids the fall of prothrombin between the second and fourth day and the variations of the prothrombin time. The author's experience shows that it cannot be hoped that vitamin K prophylaxis will avoid the hemorrhages which most commonly endanger the baby's life. Vitamin K prophylaxis is indicated in prematures in daily doses of 3 mg. for the first four days or whenever there is any infection, in infections, particularly syphilis, and in difficult deliveries and any form of fetal suffering. The most reliable prophylactic dose is 10 mg. intramuscularly to the mother during labor. The therapeutic value of vitamin K is extraordinarily reliable; normalization of the prothrombin time, even from 291 to 29 seconds within one day, is prompter than control of hemorrhage. However, vitamin K cannot be expected to control rupture of a large vessel or hemorrhage on the basis of congenital syphilis with violent manifestations in which factors other than hypopr thrombinemia play a part.

The author advises against the use oily solutions of vitamin K as they ha a tendency to cause abscesses, and stress the value of blood transfusions in suppl ing prothrombin. It should not be fo gotten that the prothrombin is lost aft three days of storage.

Acute Mastoiditis in Children Treate with Penicillin and Sulphadiazine — MOFFETT, A. J. AND DALTON, G. A. — *British Medical Journal*, 2: 1087 (N vember 12) 1949.

"It has been the practice at one ear an throat clinic at the Children's Hospital t treat as outpatients large numbers cases of mastoiditis, early or subacute, b the extensive use of the sulphonamid and penicillin in the form of an oil emu sion, reserving for admission those case which hitherto had appeared to deman immediate operation. While the possibi risks attached to this procedure laid open to criticism, the difficulties of obtain ing adequate facilities for inpatient treat ment within this or any other hospital i the vicinity were so great that it was con sidered a justifiable expedient.

"The results, however, were so satisfac tory that it was resolved to apply thi method of treatment to those cases o mastoiditis which by all previous standard demanded immediate operation. The case in this series, seen within a period of thre months, are consecutive ones in which ther could be no shadow of doubt of a clinica diagnosis of acute mastoiditis, and were treated by conservative methods. Case were selected on admission and none wa excluded on the grounds of its severity Only those in which the disease had pro gressed so far as to produce, in addition to systemic disturbances, tenderness swelling, oedema, and in some cases a fluctuating abscess over the mastoid proc ess were included in the series. All showed to a greater or lesser degree, the typical forwards and downwards displacement o the ear. . . . This, coupled with the appear ance of the drum and meatus, left no doubt of the diagnosis nor, by the usual standards, of the necessity for operation X-ray examinations were made only in the

cases in the series, and bacteriologi- examinations not at all. The latter is rtunate, because it may be that the alent invading organisms at the time cases were admitted were particularly cillin-sensitive or sulphonamide-sensi- All cases originally selected are re- ed. A careful watch was kept through- for signs of intracranial complications, none occurred."

On admission to hospital the following ne treatment was adopted: Myringot- was performed in those cases in h the drum was intact and distended. amuscular penicillin was given in ry solution, 50,000 units six hourly, in cases. In the more severe cases 100,- units were given six hourly, and in 1 50,000 units three hourly. Sulphona- s were given either four hourly or six ly, according to convenience in dosage, o a total dose varying from 10 Gm. in nts to 30 Gm. in children of 10 years over. No sulphonamide was given in se in which there was acute glomerulo- ritis. Sulphadiazine was used in most s; and mist. sulphonamide co. (con- g of sulphadiazine 37 per cent, sulpha- zole 37 per cent, and sulphamerazine per cent) in younger children. Great ntion was paid to a large fluid intake.

Local treatment consisted in careful ning of the meatus thrice daily and llation of penicillin aural drops, 10,000 s per ml. As most of the children were n from the working class districts of city, one of the most important fac- in the recovery of these cases was ubtedly the excellent nursing care and ntion to general health which they re- ed."

Response to treatment was immediately ceable in the general condition of the lren." This in the writers' opinion is most important criterion of improve- t in all acute mastoid cases. "If the l looks as if it were making progress making progress, the constitutional lition reflecting the improvement in ear. The slightly yellowish appearance he complexion reminiscent of the tint telegram envelope, easy with practice recognize but difficult to describe, lly gives way to a healthy pink. This ation in appearance is often discerni- within a few hours after treatment has begun, and precedes any obvious local change. The temperature and pulse rate fall rapidly at first and then move gradually to normal. Local changes in the ear quickly follow. The redness and tenderness rapidly disappear, the oedema subsides first, and is followed by the disappearance of fluctuation as the abscess, where the infection has burst through the bone, absorbs. The ear returns to its normal position, discharge ceases, the drum regains its colour and lustre, and hearing is restored. Many of these changes are accomplished in 48 hours, and are usually complete within a week."

The writers consider that the end results of this method of treatment, as shown by examination or replies to questions several months afterwards, are at least as satisfactory as if the cases had been operated on; and that after such a lapse of time any further ear trouble is more likely to be a reinfection than a "lighting-up" of the old one, and would be equally likely to occur in children upon whom mastoidectomy has been performed.

Epidemic Diarrhea of the Newborn — Ortega, Raul, Campos, Daniel and Quiroga, Jose C. — *Archivos del Hospital clínico de niños Roberto del Río*, 17: 47 (June) 1949.

Epidemics of diarrhea in the newborn have been reported since 1928. New York statistics show that the general decrease of infantile mortality in general and from diarrhea in particular involved only infants above the age of 1 month while the deaths from diarrhea during the first month of life showed an increase, due to the epidemics of diarrhea in the newborn. Curiously, in Chile where diarrhea of the infant is frequent, no such epidemics have been reported. Probably a new disease is not dealt with, but diarrhea of the newborn formerly was not considered separately in view of the frequency of diarrhea throughout infancy. The author believes that such epidemics have not occurred in Chile because the babies are kept with the mother in the Chilean maternity hospitals and not placed together in separate nurseries, as all epidemics so far described have occurred in nurseries. The nearest to an epidemic of diarrhea of the newborn ob-

served in Chile involved infants which were separated from their tuberculous mothers and cared for in a special ward. The syndrome was attributable to a nonspecific infection and also to infestation as shown by the findings of lambliasis and the therapeutic effect of arsenicals in 1 case, while the others responded well to sulfathiazole. Five out of 9 babies in a separate ward developed diarrhea, 4 of them separated from their tuberculous mothers and 1 premature of 2,050 Gm. separated because of hypothermia, while several prematures in the same ward did not develop diarrhea. The epidemic started with a masked case and 3 of the 5 babies involved died. The ward was closed, some of the babies were discharged, and 1 premature baby and 1 term baby were transferred to another section where babies are cared for in separate boxes. The premature baby remained free of diarrhea. The term baby was transferred at a time of frank recovery although there was still occasional slight fever and the feces still showed some alteration. At that time another baby of a tuberculous mother was admitted, with slight alteration of its feces, slight temperature elevations, and persistent explosive vomiting of biliary character, not responding to atropine, diet or anti-infectious treatment. On the sixteenth day the weight had declined from 3,350 to 2,460 Gm. and the syndrome suggested intestinal obstruction but nothing was found on laparotomy. The diarrhea which had started five to six days before operation persisted while the vomiting stopped suddenly after administration of 0.1 Gm. of seconal daily, divided into three doses. The weight increased and the bowel movements were alternately normal and diarrheic thereafter. It was suspected that this baby had been infected from the one transferred from the ward where the first epidemic had taken place and this would explain the subsequent epidemic, although the syndrome was already largely present on admission, suggesting that possibly either no epidemic diarrhea was dealt with or that this case might have been the first case of a new outbreak. Subsequently 6 more babies developed diarrhea, with 3 deaths, in spite of dietary measures and anti-infectious treatment with sulfonamides and penicillin. A definite epidemic was dealt with and it stopped when no more susceptible individuals were present. C autopsy the intestine was intact and dea was due to complications. Only in 1 ca was Salmonella demonstrable and this mu be considered the causative agent of t epidemic.

Such epidemics occurred in hospital wa perfect technics of infant care. The clin cal syndrome is one of an acute digesti disturbance, of the type of catarrh or to cosis, with loss of weight, dehydration a acidosis. Diarrhea may not supervene u til after the humoral damage has becor evident, and may be scanty. Benign i lated sporadic cases have been observ and retrospectively may have been t source of some of the epidemics. Bipha forms have been observed in which appa ent recovery was followed by sudden fa aggravation. Other infections are often e countered before or concomitantly with t epidemic diarrhea, in the same infants in the rest of the population. Cases septicemia with diarrhea should not confused with epidemic diarrhea. Epide ics have been reported in which at t same time the adults showed an epider of intestinal grippe and of poliomyeliti

A large number of different germs ha been incriminated, including *Bacillus co* Morgan's bacillus, *Proteus asiaticus, Eb thella pyogenes,* hemolytic paracolon l cilli, *Pseudomonas aeruginosa,* hemoly streptococci, *Bacillus dispar,* atypical d entery bacilli, *Streptococcus virida* enterococci, Monilia and *Salmone typhimurium.* Several writers stressed th the fecal flora of affected infants diff only slightly from that of healthy ot living under the same environmental co ditions, and assumed that the syndro may be caused by virus infection, or some systemic bacterial infection or metabolic alteration, or both togeth these factors would smooth the way intestinal proliferation of pathogenic potentially pathogenic germs. With ino lation of filtrates of the feces diarrhea a later immunity could be produced in perimental animals, suggesting a vi etiology. One observed stomatitis in old children and suggested that a virus m cause stomatitis in older children a diarrhea in the newborn; transmiss would take place by infected objects a also by adult carriers. The virus m

an attenuated vaginal infection suffi-
o infect the newborn.
epidemic which involved children and
was attributed to defects in the
milk pasteurization plant. The im-
ce of thermometers was stressed as
e of propagation. One maintained
he bottles play a part in spite of
cleanliness, and the role of furniture
aths has also been emphasized.
contagiosity varies in different epi-
s; figures between 13.4 and 37 per
ave been reported. The fatality rate
to be around 43.6 per cent on the
e, although in different epidemics it
l between zero and more than 80
ent. The results of treatment are
ore difficult to evaluate. Favorable
s were reported in 11 cases treated
succinylsulfathiazole, as compared to
ntrols. It was stated that succinyl-
hiazole and gamma globulin failed
rophylactically and therapeutically;
llin would be indicated only in com-
ons.
the basis of the literature and their
bservations the authors believe that
cial disease of the newborn is not
with and that the high morbidity
nortality are due to the fact that
rns tolerate infections poorly rather
to a special infectious agent. The
ulation of many newborns in a nurs-
eates or increases the danger of in-
; this disadvantage of the hospital
be considered when babies are tak-
a hospital because of the better equip-
for handling nutritional disturbances.
the babies are kept with the mother
eous, oral, ocular and umbilical in-
ns but no epidemic diarrhea have
observed in about 8,000 deliveries
a period of four years. Severity of
ndrome depends on disturbances of
ater metabolism and the alkaline
e rather than the diarrhea, and the
may be slight or absent. Thus a
c or nonspecific infection is dealt
provoking the humoral syndrome be-
of the physiologic hydrolability of
ewborn, and the term of epidemic
ea is ill chosen; however it has gain-
de acceptance and it seems useful
k to it as a prophylactic criterion,
with the etiopathogenetic reserves
d out.

Management of the Premature Baby—MONCRIEFF, ALAN — *British Medical Journal*, 2: 1104 (November 12) 1949.

"If premature labour has set in and a small baby is expected certain preliminary steps can be taken. It is wise to give the mother a dose of vitamin K. A cot or basket should be prepared with lined sides to prevent draughts. If time permits an oxygen cylinder should be obtained, with a close-fitting rubber mask or a nasal catheter for administration.

"After the baby is born it should be wrapped in a warm towel and placed head downwards in the cot or basket, which should be suitably tilted. Gentle wiping out of the mouth and gentle aspiration with a rubber catheter will make sure that the air passages are clear. If available, oxygen may be administered for a short period to produce a good saturation of the arterial blood. If respiration is feeble carbon dioxide from a 'sparklet' apparatus may be used, or some device improvised to secure a degree of rebreathing.

"It must be remembered from the start that the greatest enemy is infection, and in the early days the nurse and doctor should wear an efficient mask and conduct all manipulations with an aseptic or antiseptic technique.

"The room in which the baby is to be nursed must be kept warm—70 to 75° F. is ideal—in addition to the careful use of hot water bottles in the cot or the employment of an electric blanket pad (which can be hired in some areas). The aim is to keep the baby's rectal temperature not below about 98° F., but this is sometimes not achieved for a few days. The temperature should certainly be taken and recorded four hourly. The atmosphere must also be kept moist enough to minimize 'evaporation' from the baby's skin and lungs. A wet towel hung over the back of the chair, with its end in a bowl of water and placed near a source of heat, will provide a reasonable degree of humidity. A bathroom, if available and able to be temporarily set apart for the baby, is often ideal because of its humidity.

"When the baby has recovered from the initial shock and is breathing well and has a good colour the nurse may give it a gentle cleansing. This is most efficiently accomplished as a modified blanket bath

with soap and water and a soft flannel, exposing only a small portion of the skin at a time. Drying should be carried out by gentle dabbing with a warm, soft towel, followed by a suitable baby powder (olive oil is messy, an inefficient cleaning agent, and not always sterile). The normal procedures for care of the eyes and cord should be carried out. Napkins can be applied, and the baby dressed in a gamgee jacket, bootees, gloves, and a bonnet, leaving only the face exposed. The bedclothes must not be too heavy. Before this dressing-up, however, the weight should be obtained if the baby's condition permits, for it is a most valuable base line from which to judge subsequent progress. The infant should now be left in its cot and disturbed as little as possible, except to be moved from one side to the other from time to time to promote full expansion of the lungs. Oxygen may still be required at intervals if the colour does not remain good.

"All these measures are necessary at first, but from the start the programme of management must be designed to speed up the process of maturation. That is to say, the baby must be brought daily nearer to the normal standards of care of the full time infant. The external temperature of the room can be gradually lowered, some of the gamgee clothing cut away, and hot water bottles or blanket pad left out of the cot for brief but increasing periods. It is difficult to lay down precise details to cover premature babies of all weights. Careful judgment is required, and the experience of the nurse is invaluable." The writer stresses the necessity for making progress and not keeping the baby too long before his own heat-regulating mechanism is called upon to take action.

"The same difficulty over precise details arises in connexion with feeding. Certain general principles will be discussed and, as far as possible, their application to a group of infants whose weights range from 2 pounds or less up to the official standard of 5 1/2 pounds.

"Methods.—Most premature infants are too weak at first to suck at the breast, so that easier methods must be tried. In order of decreasing strain on the baby, after breast feeding these are: sucking at an ordinary bottle; the use of a Breck feeder (a small bottle with a rubber nozzle at the end opposite the teat, like the o fashioned fountain pen filler, by wh positive pressure can be exerted); a spo or pipette to drop the feed into the mou or tube feeding by a catheter passed do the oesophagus through either the nose mouth.

"The first thing to establish after baby is born is whether or not he c swallow. A little sterile water from a spo can be tried. If there is no swallowing flex, tube feeding will clearly be necessa If the baby can swallow, the next thi to ascertain is whether or not sucking c be carried out. If sucking proves possi a Breck feeder is the simplest apparatu if not, a spoon or tube should be used cording to the ability to swallow. The perienced nurse can soon determine a w of mixing the methods of feeding—one two tube feeds and the rest by spoon, starting the feed with a bottle and fini ing with a spoon when the baby gets ti of sucking. Here, too, progress must made and each day should see an atte to take the baby a stage up the scale tube, spoon, bottle—with the object getting him to the breast.

"Feeds.—Breast milk is the safest a most easily digested food. All prematu babies should receive it at first even if cannot always be continued. For the fi 24 hours sterile water in small sips sho be used, and during this period efforts secure a supply of breast milk can be ma Only a few ounces a day will be requi at first and should be obtainable witho much difficulty from any nursing mot or from a maternity unit. It should boiled and diluted to one-fourth streng for the very small babies and to one-h strength for the medium and larger-siz infants. Meanwhile the baby's own mo er's supply of colostrum and milk sho be obtained by manual expression.

"By the end of a week or 10 days breast milk can be given undiluted. I supply proves impossible to obtain a no more can be got from the baby's o mother an alternative has reluctantly be used. To avoid subsequent change choice should be made of a dried mi either one of the so-called humanized rieties or a half-cream brand. These dr milks have the additional advantage being obtainable at the local welfare cen

er of these milks can be given from second or third day of life and in a ion which may vary from an eighth arter-strength, according to the baby's up to half-strength. One measure of powder to an ounce (30 ml.) of water be assumed to be full strength. An ncpt should be made to increase the gth daily, aiming eventually—in the nd or third week—at full strength for humanized brand and three measures ounces for the half-cream variety.

For simplicity, the addition of sub- ces to the milk is not recommended. e authorities prescribe additions of ble casein and others prefer to use orated milk, sweetened or unsweeten- but the programme outlined above s well and, as has been said, mini- s changes when the infant is older.

Times of Feeding.—Quantities and in- ls of feeding are related. It must be mbered that small babies require rela- y more food than full term infants. he basis for a 7 pound baby is 2 1/2 es of breast milk per pound (150 ml. Kg.) body weight per day, then the ler infant may require as much as 1/2, or even 4 ounces per pound be- a steady weight gain is achieved. But, with normal babies, such a full feed ramme should not be attained too kly. If the largest feed, in volume, is eved by the seventh to tenth day, this ually safe. If dried cow's milk is being progress should be slower and for smallest babies the full size (and gth) not reached until a little later. vided that no oedema develops the ht curve is a most valuable guide and experienced nurse can increase the gth and size of the feeds to keep pace the strength and requirements of the nt. With the smallest infants this will lly mean beginning with feeds of 30 0 minims (1.8-3.5 ml.) every hour by and two hourly by night. Gradually is increased to 1/2 ounce two hourly day and three hourly by night, until nce is taken every three hours round clock. If the mother's milk supply has established the infant may be tried he breast at least once a day if over unds in weight at birth, or when this ht is achieved. Even smaller babies, cially if twins (and therefore relatively more mature than the weight indicates), can suck quite strongly under this weight.

"Whatever the feed a start should be made with vitamin supplements when the infant is a month old. Vitamin C as ascorbic acid in 25 mg. daily dosage can safely be given even before this. Vitamins A and D are best given as a vitamin concentrate to allow 1,000 to 2,000 units of vitamin D daily, and such dosage—twice the requirements for a full term baby—should be continued throughout the first year. Iron is also best administered early, say at two to three months, and given in Mackay's mixture in a dosage of 1 grain (65 mg.) three times a day.

"Two other medicaments are also worthy of mention. Some paediatricians give all babies vitamin K after birth to prevent hypoprothrombinaemia, and, as already suggested above, if premature labour is anticipated this vitamin can be given to the mother also. Thyroid extract has a useful part to play. If the baby is particularly sluggish and difficult to rouse and has a subnormal temperature, the metabolism can certainly be stimulated by giving the equivalent of 1/10 grain of thyroid extract per pound (14.4 mg. per Kg.) body weight daily. This should generally be administered for a few days only, after which the increased food intake will itself stimulate metabolism.

"Thyroid extract is the only safe stimulant for the premature baby. Brandy appears to be used fairly frequently, but it is irritating to the stomach and intestines and if given in stimulating dosage may produce a dangerous gastroenteritis. If the baby is kept adequately warm and gently handled brandy should be unnecessary."

Clinical Observations in Meningococcic Meningitis — Domínguez Recio, M. — *Boletín del Instituto de Patología médica*, 4: 170 (September) 1949.

The author reports observations on an epidemic of 34 cases of meningococcic meningitis. There are considerable variations in the clinical picture of this infection in different epidemics. In the epidemic dealt with by the author a sudden onset was characteristic, with pallor, fever, and particularly vomiting which was repeated and intense. In almost all cases mental

changes occurred immediately being mostly stupor and less frequently agitation and marked hyperesthesia. In children between the ages of 2 and 5 convulsions are a late symptom and do not occur with early treatment. In infants, however, convulsions occur early, but are limited at first to rapid clonic contractions of the facial muscles and therefore requires careful observation, while generalized convulsions usually appear later. In infants the fontanels will usually bulge unless there is associated marked dehydration. Clonus was frequently observed.

Among the meningeal signs Brudzinski's sign appears before Kernig's and before nuchal rigidity. Marañon's sign was observed in 12, Flatu's in 4, and positive dermographism in 5 cases. There was pupillary asymmetry in 3, pupillary sluggishness to light in 4, and lack of pupillary reaction in 1 case. Only 1 patient showed strabism and hemiparesis which subsided in the course of treatment. Brudzinski's contralateral sign was not frequent. Urinary retention is frequent in adults but was not observed among the children of this epidemic; it was observed as the first manifestation of tuberculous meningitis in 1 case. Herpes was observed in 9 cases, always between the second and fourth day, and particularly in older children; no herpes outside the face was observed. Extensive cutaneous petechiae and hemorrhages, apparently indicating a septicemic condition, were observed in 14 children; they appeared at the same time as the meningeal signs, except in 1 case in which they appeared after 36 hours. Five of these children presented a complete Waterhouse-Friderichsen syndrome, with petechiae, purpura, intense pallor, cyanosis, hypotension, tachycardia, dyspnea of a respiratory and metabolic character like in acidosis, and wet pulmonary findings, while intense abdominal pain was present in only 1 of them, associated with muscle rigidity and creating the impression of an acute abdominal syndrome. Definite hypertrophy of the thymus was present in only 1 child, and a history of exudative diathesis in 2; the age range was between 2 1/2 and 5. The Waterhouse-Friderichsen syndrome is usually caused by meningococcic infection but may be caused by other infections; the author observed a case of bilateral suprarenal hemorrhage in a pneumobacillus septicemia, but nothing could be said about the clinical manifestations as the patient had died during the night without appreciable prodromal symptoms. Some authors consider the Waterhouse-Friderichsen syndrome and meningococcic meningitis as stages of the same process, the former sometimes developing so rapidly that no meningeal syndrome develops; meningeal symptoms and generalized convulsions are rare at the onset. There is considerable doubt whether death is actually due to suprarenal hemorrhage, as, suprarenalectomized animals develop the symptoms only after a relatively long interval, as some patients recover, and as identical syndromes may occur in the absence of suprarenal hemorrhages; in 1 case reported suprarenal lesions were absent while the pituitary showed necrotic areas. The prognosis has improved with early recognition and appropriate treatment.

There was only 1 death in the author's 5 cases, and in this case treatment had not been started until 18 hours after onset; death supervened 12 hours later. In the remaining cases treatment was instituted within four hours. Treatment is chiefly based on combating the infection, and the favorable results were obtained although the cortical hormone was not given in abundant amounts.

In all but 5 cases in children above the age of 5 the author observed a characteristic position in meningococcic meningitis; namely, supine decubitus with lateral inclination of the head to the side on which the lower limb was held in flexion; this kitten-like position was regularly found during the first few hours.

The spinal fluid showed the classical findings; only in the case of Waterhouse-Friderichsen syndrome with the picture of an acute abdominal syndrome, it was so thick that it coagulated in the needle preventing further withdrawal in spite of an attempt of dilution with saline solution. On the first day it contained the germs in all but 1 of the cases. There was absolute parallelism between disappearance of the clinical symptoms and normalization of the spinal fluid, except that hypertension of the latter persisted in some cases.

Treatment was based on a combination of sulfathiazole and penicillin, the former in a dose of 0.3 Gm. per Kg. and the latter in a dose of 15,000 to 30,000 units every three hours; intraspinal penicillin treatment did not seem to be of any special advantage and caused elevations of temperature; it was therefore discarded. Treatment also included cortical extract, high doses of vitamin C (500 mg. daily), and appropriate symptomatic medication. Fluids were given parenterally when indicated by dehydration or intense vomiting.

The average duration of the disease was one to two weeks, except in 1 girl, aged 12, in whom sulfathiazole had to be discontinued because of intolerance and cure was achieved within six days with penicillin alone. There were 2 deaths, 1 from Waterhouse-Friderichsen syndrome, and the other from a dysenteriform colitis after cure of the meningitis.

Symposium Section

Etiology of Rheumatic Fever

The dramatic success obtained by Hench, Kendall and others with cortisone and ACTH in rheumatic conditions does not make it inappropriate to discuss current progress of studies which may lead to a better concept of their etiology. In this connection we were very impressed with the Kober Lecture which was delivered by Dr. Homer F. Swift of the Hospital of the Rockefeller Institute for Medical Research. This lecture was first delivered at Georgetown University Medical Center last March and was repeated in part before the American College of Physicians in New York City in April. It has just been printed in the *Annals of Internal Medicine*.[1]

The opening sentence of the first paragraph as well as what follows in this paragraph is what attracted the attention of those who have been interested in and have followed the long and painstaking studies in an effort to discover the etiology of rheumatic fever. Dr. Swift calls attention to the widespread acceptance of the role of streptococcic infections in rheumatic fever, although the evidence for this opinion still seems insufficient for the hypercritical. Concerning this he believes that there are at least three attitudes: "(1) acceptance of the thesis and a readiness to apply it practically to public health aspects of the problem; (2) relative indifference to the information that has been laboriously collected and correlated; (3) skepticism and reiteration of the statement that the cause of this disease is unknown, or claims that an unidentified virus is the offending agent."

What follows in Dr. Swift's discussion of these three attitudes cannot be included here, excepting in part, so we commend the reading of the original text of the lecture to anyone, regardless of their support of the attitudes advanced. We were particularly impressed with the second, which concerns the relative indifference to the information "so laboriously collected and correlated." This is because of the fact that anyone who has collected and classified medical literature is frequently impressed with the failure of many to read what the "moving finger writes; and having writ, moves on." This may be due to many reasons, but the failure to read the writing of those who have moved on is so often expensive in labor, time and money. So, if this "relative indifference to the information that has been laboriously collected and correlated" did not exist, it would be possible to discover that many obstacles had been removed from the path toward a goal and a trail had been blazed for our convenience. While many do accept and believe in the part played by streptococcic infection in rheumatic states, some of the skepticism which they hold could be lessened by reading a lecture such as Dr. Swift has delivered on two occasions. He has lived through a period when the greatest effort has been made to establish the specificity of one or more strains of streptococci as a cause of rheumatic conditions and has contributed generously to the study.

Swift contends that the perusal of patients' histories for almost two centuries reveals descriptions of cases of acute articular rheumatism that followed closely in the wake of a severe throat. This observation has been made down to the present time. Consequently the bacteriology of the throat has been diligently studied by many but the number of organisms which comprise its bacterial flora and the changes which so frequently occur has made it difficult to decide on any one of them as a specific cause. Cultural methods by which the organisms could be studied were unsatisfactory, confusion concerning strains of organisms and the discovery that polyarthritis could be caused by organisms like the gonococcus added to this difficulty.

1. Swift, H. F.: The Etiology of Rheumatic Fever, *Ann. Int. Med.*, **31**:715 (November) 1949.

Streptococci usually outnumbered the ners in most cultures from the throat, it was high on the list of suspicious ganisms. It was, however, difficult at the ne to separate the hemolytic from the nhemolytic streptococci, so the early ims of the pioneers, Poynton and Paine Great Ormond Street Hospital for Sick ildren, concerning the role of the strep- cocci in the rheumatic fevers in children re open to criticism. Swift's suggestion s that their bacteriologic data indicate at in some cases they were dealing with *reptococcus pyogenes* septicemia termi- lly complicating genuine rheumatic ver, and in others, with subacute bac- rial endocarditis superimposed on old eumatic scarred valves. Consequently, ile they did start the thinking that a eptococcus was the most suspicious ganism, they were unable in their time refute the criticism of their work.

Perhaps the greatest encouragement to e students of the elusive streptococci me in 1903 when Schottmüller brought th his blood agar technic for distinguish- g hemolytic from nonhemolytic strep- cocci, and found that the hemolytic ains were the more virulent. It seems credible that this technic was not utilized Poynton and Paine, whose work was t reported until 10 years later. The me tardiness in adopting it seemed to ply to many others. This may have been e to the fact that so many were engaged a controversy over their own or some her individual's strain. Somewhere ring the controversy came the conten- n, as mentioned by Swift in the open- g paragraph of his lecture, that a virus s the true cause. Then the situation ally became complicated.

Meanwhile, studies of the strains of eptococci were not neglected. In fact nsiderable order came out of the chaos the second decade of the century. The st World War accelerated studies just did the second. The streptococci were rticularly troublesome in the measles eumonias, scarlet fever and in the em- ema, pericarditis and endocarditis which llowed. Again subsequent arthritic dis- ses were conspicuous in following strep- tococcic sore throat. So in addition to blaming the streptococci for many diseases, interest was again aroused in their relation to rheumatic conditions.

Around the beginning of the last decade of the half century the discoveries of Lancefield and her associates in the laboratories of the Rockefeller Institute of Medical Research clarified the chaotic atmosphere. Contributing to this, Swift recognizes the work of Griffith in London. As a result of these discoveries the existence of at least 12 serologically recognizable groups has been demonstrated. In addition ungrouped viridans varieties are recognized. So again the opportunity for experimental studies has been created. This time they have already been and will continue to be conducted with organisms which are more perfectly understood.

Dr. Swift has discussed some of the experimental studies which have been made possible by the work of Lancefield and her associates. What has been presented in the Kober Lecture must be considered only in the nature of a preview. Definite conclusions have not been drawn and results so far must remain unpredictable. Nevertheless they are encouraging and hopeful.

In any event advantage has been taken of a very considerable amount of information which has been laboriously collected and correlated, just as Domagk did when he gave the world prontosil after he re-examined the laboriously accumulated information left by Paul Ehrlich, or as Florey and Chain did when they were curious enough to try to find out if it was possible to treat infections with some of the material which Fleming casually observed was capable of destroying staphylococcus colonies adjacent to contaminating molds on discarded petri dish cultures. Maybe someone will discover why rheumatic conditions follow a sore throat.

Meanwhile let us not forget that to the end of time there will always be opportunity beyond the horizon for those who seek it—but occasionally they should look backward to see if they cannot finish the work of those whose ambitions were never realized because there was so little time—or it was later than they thought.

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Duck Eggs

When the average American orders ham and eggs he expects and usually gets hen eggs. Rarely, if ever, does he get duck eggs and if he did he would probably detect a different taste and might even suspect that the order was filled with overripe eggs or those from an elderly hen. As a matter of fact we have not heard of duck eggs being used for any other purpose than hatching in recent years. Some years ago we can recall that they were used in bakeries where their definitely objectionable taste could be concealed only by other flavorous ingredients which made the products of these emporiums delectable to the public. But in recent years we have not heard that they have been used. This is probably due to the fact that need for using them does not exist. Consequently we have never been confronted with the fact that duck eggs are or may be dangerous to humans.

In less fortunate countries than ours they have been used just as we use hen eggs. The fact that they are capable of causing enteritis which has caused death is not widely known to us. The first time[1] we learned of the occasional dangers of duck eggs was in 1932 when the British Ministry of Health reported on their investigation of 3 separate cases of food poisoning, 1 of which was fatal, that were caused by eating duck eggs. At the time this source of food poisoning was regarded as being extraordinary but in discussing it in these columns we find that we recorded that "the *Bacillus aertrycke* (*Salmonella aertrycke*) was isolated from the human cases, and eggs infected with the same bacillus were obtained from the corresponding flocks of ducks." Furthermore it was stated in the report of the Ministry of Health that, "by agglutination tests on the blood, 18 birds in a flock of 46 proved to be infected, and at least 4 of these laid infected eggs." In another place all out of 9 were infected and in a third, 2 out of 5.

Again in 1939 reports of two epidemics of enteritis among troops came from Germany. It involved 65 in one epidemic and 138 in another.

Exactly how ducks become infected is not known, but their well known filthy habits of grouting about in mud and garbage, unless they are confined in cleaner areas, may be a contributing factor. Ordinarily salmonella organisms are harbored by rats and mice who have been known to contaminate food and otherwise spread the organisms.

Elsewhere* in this issue we have abstracted the report of a hospital outbreak in England. This was caused by serving a dish known as a "queen of puddings." Inquiry in the kitchen revealed that this lightly cooked pudding had been made with 200 duck eggs and had been served to the nursing and other staff members as well as a few of the patients. The details of this outbreak are given in the abstract. Stool cultures showed the presence of *Salmonella typhimurium*.

It seems to be well established now over a period of many years that duck eggs are capable of containing pathogenic organisms of the salmonella group and some risk is involved in eating these eggs unless they are thoroughly cooked. Hen eggs have been known to contain salmonella organisms but improvement in flocks of hens in America by public health and veterinary groups has practically eliminated this danger.

1. Editorial: Ducks' Eggs, *Internat. M. Digest*, **21**: 254 (October) 1932; *ibid.*, **34**: 126 (February) 1939.

* Page 72.

A Third Coronary Artery

t is conceivable that some encourage-
nt will be derived by those who have
reason to be concerned about the blood
ply to their heart, from a study re-
ted from the Departments of Medicine
Pathology of Harvard University
ch establishes a new source of blood
the hearts of many individuals. This
rmation was obtained by Schlesinger,
and Wessler[1] from a study of 651
nan hearts in 50 per cent of which they
d that the portion of the right ventricle
wn as the area of the conus arteriosus
a unique arterial blood supply through
ssel accessory to the two conventional
nary arteries. The supernumerary ves-
in this region, which these investigators
e called the "conus artery," arises by
parate orifice behind the right aortic
e cusp, courses over the anterosuperior
ace of the right ventricle, and termi-
s near the anterior interventricular
ve.

his Harvard team found that super-
nerary coronary arteries have been ob-
ed since the days of the early anat-
sts, but as they have received little
ntion in most modern anatomic text-
ks and are usually considered as un-
mon variations of little significance
two main coronary arteries have been
sidered the chief source of blood for
main pumping station for the rest of
human anatomy.

he human hearts on which the obser-
ons are based were all prepared by a
hod of injection plus dissection pre-
sly reported by Schlesinger.[2] Briefly
consists of injecting a radiopaque lead-
mass of different colors into the two
n coronary arteries, "unrolling" the
t so that its entire arterial tree lies in
plane, taking a roentgenogram of the
lled heart, and carefully dissecting the
nary arteries, using the film as a guide.
s technic discloses the narrowings, oc-
ions and anastomoses in the roentgen-
phic visualized coronary arteries in
y heart. As a result the conus artery attracted the attention of these observers in routine injections by this method, when the injection mass occasionally filled the conus artery by anastomotic pathways and leaked through its mouth into the aorta. Their total series comprised 1,000 hearts but only 651 were used in their analysis because the others were rejected on account of unsatisfactory observations on the conus artery.

There are, in this article, five roentgenograms of injected hearts which have been unrolled and spread flat so that the entire vascular area is clearly shown in one plane. In addition more graphic tracings are shown beneath each roentgenogram so that areas and delineation of the vessels are defined by lettered labels. Thus single and double conus arteries are easily seen and boldly defined in one half of the 651 human hearts which were considered worthy of analysis. The vessel varies considerably in size. It may range from 0.4 to 1 mm. in internal diameter at its origin and may reach a diameter of 2 mm. or more.

It is, of course, not possible to evaluate the significance of this artery at so early a period but the discoverers do emphasize a few points which they have brought out in their graphic demonstration of its existence. For example, they have observed that although the conus artery arises directly from the aorta, it does not have the high incidence of occlusion found in the first 4 cm. of the coronary artery trunks. This they construe as lending no support to the concept that the higher incidence of occlusions near the origin of the main coronary arteries is, in some way, related to the presumably higher blood pressure in this portion of these vessels. Its separate origin results in its independence of obstruction so often found at or near the mouth of the right coronary artery, and affecting its first ventricular branch. In addition, its independent communication with the aorta and its location between the main left descending and the right coronary arteries make it a ready source of anastomotic connection between the aorta and the coronary arterial tree distal to the zones in which the incidence of occlusions is highest. Furthermore, the low incidence of occlusion in the conus artery, lower than in any other coronary artery directly

[1] Schlesinger, M. J., Zoll, P. M. and Wessler, S.: The Conus Artery: a Third Coronary Artery, *Am. Heart J.*, **38**:823 (December) 1949.

[2] Schlesinger, M. J.: An Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses, *Am. Heart J.*, **15**:528 (May) 1938.

connected with the aorta, enhances its value as an effective pathway and source of collateral blood supply. In the presence of old occlusions anywhere in the heart muscle, the discoverers suggest that the incidence of anastomoses with the conus artery increases threefold. This unique vessel responds to the need for increased blood supply as if it were an accessory artery strategically placed between the left descending and right coronary arteries, which supply most of the blood in most human hearts. So it is reasonable to assume that the clinical consequence of occlusion in these two coronary arteries may be significantly influenced by the presence or absence of a conus artery.

The information concerning the blood supply to the human heart through the conus artery which is entirely independent of the other two sources will be received with interest. This painstaking and convincing study may prove to be as epochal as the discovery of the significance of coronary thrombosis. It will probably not have any effect on the incidence of this cause of heart failure but it is comforting to know that about 50 per cent of us have three strikes before we are out.

In his fifteenth annual review of the significant publications on Infectious Diseases, Hobart A. Reimann of Jefferson Medical College and Hospital, calls attention to the fact that the records of the Metropolitan Life Insurance Company indicate that for five successive years there has been an uninterrupted decline in the mortality rate for infectious diseases. An "all time low" mortality rate has been established for 1948 and a "record-breaking low" for the first six months of 1949. There has been a drop of 22 per cent in the death rate from tuberculosis in two years. Scarlet fever, diphtheria, whooping cough, syphilis, enteritis, pneumonia, and influenza have the lowest death rates ever recorded. That for pneumonia is 40 per cent below the average for the 10 year period of 1938 through 1947. Much of the decline in mortality from the diseases mentioned is due to the successful specific therapy or prophylaxis now available. On the other hand, the number of cases of poliomyelitis was exceeded only once before, in 1916. This increase may be due partly to better diagnosis and to better reporting of cases.—*Archives of Internal Medicine,* 85: 156 (January) 1950.